

Paul Schulwitz

Access DB# 112156

# SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name Rebena Look Examiner # 69826 Date: 1/14/04  
Art Unit 1664 Phone Number 30 \_\_\_\_\_ Serial Number: 09/928911  
Mail Box and Bldg/Room Location unt Results Format Preferred (circle) PAPER DISK E-MAIL  
2001

If more than one search is submitted, please prioritize searches in order of need.

\*\*\*\*\*  
Please provide a detailed statement of the search topic and describe as specifically as possible the subject matter to be searched include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: \_\_\_\_\_

Inventors (please provide full names): Mark Zarowski

Earliest Priority Filing Date: 8/11/98

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please provide structures for tricothecene & search them for ~~method~~ of claims ~~part~~ 9410

Thank you  
Rebena Look

Rush Search Approved  
TK Page  
SPE, AV 1655

## STAFF USE ONLY

Staff Use Only	Type of Search	Vendors and cost where applicable
Searcher: <u>JARREL 10'00'PCW</u>	NA Sequence (#) _____	STN: <u>499</u>
Searcher Phone # _____	AA Sequence (#) _____	Dialog _____
Searcher Location _____	Structure (#) _____	Questel Orbit _____
Date Searcher Provided _____	Bibliographic _____	Orbit _____
Date Completed: <u>1/15/04</u>	Litigation _____	Lexis Nexis _____
Searcher Prep & Review Time: <u>64</u>	Fulltext _____	Sequence Systems _____
Client Prep Time _____	Patent Family _____	WWW Internet _____
Waiting Time: <u>116</u>	Other _____	Other (specify) _____

=> b reg

FILE 'REGISTRY' ENTERED AT 10:58:37 ON 15 JAN 2004  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 13 JAN 2004 HIGHEST RN 637299-19-5  
DICTIONARY FILE UPDATES: 13 JAN 2004 HIGHEST RN 637299-19-5

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
information enter HELP PROP at an arrow prompt in the file or refer  
to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

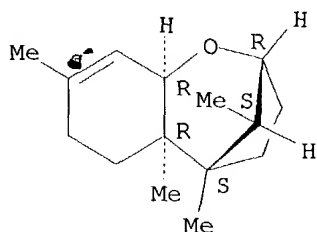
=> d que 19

L7 1 SEA FILE=REGISTRY ABB=ON PLU=ON TRICHOTHECENE/CN  
L8 1 SEA FILE=REGISTRY ABB=ON PLU=ON TRICHODERMIN/CN  
L9 2 SEA FILE=REGISTRY ABB=ON PLU=ON (L7 OR L8)

=> d ide 19 tot

L9 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 51724-48-2 REGISTRY  
CN Trichothec-9-ene (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 2,5-Methano-1-benzoxepin, trichothec-9-ene deriv.  
OTHER NAMES:  
CN **Trichothecene**  
FS STEREOSEARCH  
DR 66187-00-6  
MF C15 H24 O  
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN,  
CIN, EMBASE, IPA, PROMT, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.



**\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\***

168 REFERENCES IN FILE CA (1907 TO DATE)  
65 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
169 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN

RN 4682-50-2 REGISTRY

CN Trichothec-9-en-4-ol, 12,13-epoxy-, acetate, (4 $\beta$ )- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Spiro[2,5-methano-1-benzoxepin-10,2'-oxirane], trichothec-9-en-4-ol deriv.

CN **Trichodermin (7CI)**

CN Trichothec-9-en-4 $\beta$ -ol, 12,13-epoxy-, acetate (8CI)

OTHER NAMES:

CN NSC 267033

CN NSC 73846

CN WG 696

FS STEREOSEARCH

DR 11010-11-0, 16821-99-1

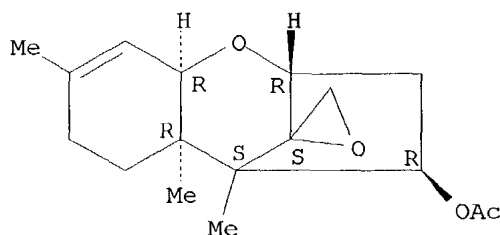
MF C17 H24 O4

CI COM

LC STN Files: AGRICOLA, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CSCHM, DDFU, DRUGU, EMBASE, MEDLINE, MRCK\*, NAPRALERT, NIOSHTIC, RTECS\*, SPECINFO, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)

*This is a type of trichothecene according to Medline*

Absolute stereochemistry.



**\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\***

128 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
129 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> => b cap

FILE 'CAPLUS' ENTERED AT 13:38:24 ON 15 JAN 2004

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FILE COVERS 1907 - 15 Jan 2004 VOL 140 ISS 3  
FILE LAST UPDATED: 14 Jan 2004 (20040114/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que 139

```

L7      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICOTHECENE/CN
L8      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHODERMIN/CN
L9      2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L7 OR L8)
L10     293 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9
L12     22658 SEA FILE=CAPLUS ABB=ON  PLU=ON  LUNG, NEOPLASM/CT
L13     235 SEA FILE=CAPLUS ABB=ON  PLU=ON  LUNGS, NEOPLASMS/CT
L15     125489 SEA FILE=CAPLUS ABB=ON  PLU=ON  LUNG#/OBI OR PULMON?/OBI
L28     596051 SEA FILE=CAPLUS ABB=ON  PLU=ON  CANCER?/OBI OR MALIGN?/OBI OR
        NEOPLAS?/OBI OR TUMOR?/OBI OR TUMOUR?/OBI OR CARCINO?/OBI OR
        ADENO?/OBI OR SARCOMA?/OBI
L32     2241 SEA FILE=CAPLUS ABB=ON  PLU=ON  TRICOTHEC!NE#/OBI OR TRICHODER
        MIN#/OBI OR T-2/OBI (W) TOXIN/OBI OR (NSC/OBI (W) 267033/OBI
        OR 73846/OBI) OR WG/OBI (W) 696/OBI
L33     4 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L10 OR L32) AND L28 AND L15
L38     1 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L10 OR L32) AND (L12 OR L13)
L39     4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L33 OR L38

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=> b uspatfull

FILE 'USPATFULL' ENTERED AT 13:38:41 ON 15 JAN 2004  
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 15 Jan 2004 (20040115/PD)  
FILE LAST UPDATED: 15 Jan 2004 (20040115/ED)  
HIGHEST GRANTED PATENT NUMBER: US6678893  
HIGHEST APPLICATION PUBLICATION NUMBER: US2004010831  
CA INDEXING IS CURRENT THROUGH 15 Jan 2004 (20040115/UPCA)  
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 15 Jan 2004 (20040115/PD)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2003  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2003

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>>> USPAT2 is now available.  USPATFULL contains full text of the  <<<
>>> original, i.e., the earliest published granted patents or      <<<
>>> applications.  USPAT2 contains full text of the latest US      <<<
>>> publications, starting in 2001, for the inventions covered in   <<<
>>> USPATFULL.  A USPATFULL record contains not only the original  <<<
>>> published document but also a list of any subsequent            <<<
>>> publications.  The publication number, patent kind code, and    <<<
>>> publication date for all the US publications for an invention   <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<

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*Combo of Lung (FT), ~~CT~~ Lung Cancer (FT, CT) and (Structure) Rn, PT*

>>> records and may be searched in standard search fields, e.g., /PN, <<<  
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<  
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<  
>>> enter this cluster. <<<  
>>> <<<  
>>> Use USPATALL when searching terms such as patent assignees, <<<  
>>> classifications, or claims, that may potentially change from <<<  
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> d que 137

```
L7      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHOTHECENE/CN
L8      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHODERMIN/CN
L9      2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L7 OR L8)
L20     19 SEA FILE=USPATFULL ABB=ON  PLU=ON  L9
L22     3559 SEA FILE=USPATFULL ABB=ON  PLU=ON  LUNG, NEOPLASM/CT
L24     45842 SEA FILE=USPATFULL ABB=ON  PLU=ON  (CANCER? OR MALIGN? OR
        NEOPLAS? OR TUMOR? OR TUMOUR? OR CARCINO? OR ADENO? OR
        SARCOMA?)/TI,IT,AB,CLM
L25     15008 SEA FILE=USPATFULL ABB=ON  PLU=ON  (LUNG# OR PULMON?)/TI,IT,AB,
        CLM
L34     78 SEA FILE=USPATFULL ABB=ON  PLU=ON  (TRICHOTHEC!NE# OR TRICHODER
        MIN# OR T-2 (W) TOXIN OR (NSC (W) 267033 OR 73846) OR WG (W)
        696)/TI,IT,AB,CLM
L35     2 SEA FILE=USPATFULL ABB=ON  PLU=ON  (L34 OR L20) AND L24 AND
        L25
L36     0 SEA FILE=USPATFULL ABB=ON  PLU=ON  (L34 OR L20) AND L22
L37     2 SEA FILE=USPATFULL ABB=ON  PLU=ON  (L35 OR L36)
```

COMBO OF COMPOUNDS (FT, RN) AND LUNG CANCER

=> b medline cancerlit

FILE 'MEDLINE' ENTERED AT 13:38:58 ON 15 JAN 2004

FILE 'CANCERLIT' ENTERED AT 13:38:58 ON 15 JAN 2004

=> d que 146

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L7      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHOTHECENE/CN
L8      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHODERMIN/CN
L9      2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L7 OR L8)
L40     52 SEA FILE=MEDLINE ABB=ON  PLU=ON  L9
L41     1956 SEA FILE=MEDLINE ABB=ON  PLU=ON  TRICHOTHEC!NE# OR TRICHODERMIN
        # OR T-2 (W) TOXIN OR (NSC (W) 267033 OR 73846) OR WG (W) 696
L42     1724 SEA FILE=MEDLINE ABB=ON  PLU=ON  TRICHOTHECENES+NT/CT
L43     91408 SEA FILE=MEDLINE ABB=ON  PLU=ON  LUNG NEOPLASMS+NT/CT
L44     1 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L40 OR L41 OR L42) AND L43
L45     1 SEA FILE=CANCERLIT ABB=ON  PLU=ON  (L40 OR L41 OR L42) AND L43
L46     1 SEA FILE=CANCERLIT ABB=ON  PLU=ON  (L44 OR L45)
```

COMBO OF COMPOUNDS (FT, RN) AND LUNG CANCER

=> b embase

FILE 'EMBASE' ENTERED AT 13:39:13 ON 15 JAN 2004

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FILE COVERS 1974 TO 5 Jan 2004 (20040105/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 169

```

L7      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHOTHECENE/CN
L8      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHODERMIN/CN
L9      2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L7 OR L8)
L62     432 SEA FILE=EMBASE ABB=ON  PLU=ON  L9
L63     128236 SEA FILE=EMBASE ABB=ON  PLU=ON  (CANCER? OR MALIGN? OR
NEOPLAS? OR TUMOR? OR TUMOUR? OR CARCINO? OR ADENO? OR
SARCOMA?) AND (LUNG# OR PULMON?)
L64     1415 SEA FILE=EMBASE ABB=ON  PLU=ON  TRICHOTHEC!NE# OR T-2 (W)
TOXIN OR TRICHODERMIN# OR (NSC (W) 267033 OR 73846) OR WG (W)
696
L65     4 SEA FILE=EMBASE ABB=ON  PLU=ON  (L62 OR L64) AND L63
L66     5592 SEA FILE=EMBASE ABB=ON  PLU=ON  LUNG TUMOR/CT
L67     71146 SEA FILE=EMBASE ABB=ON  PLU=ON  LUNG CANCER+NT/CT
L68     1 SEA FILE=EMBASE ABB=ON  PLU=ON  (L66 OR L67) AND (L62 OR L64)
L69     4 SEA FILE=EMBASE ABB=ON  PLU=ON  L65 OR L68

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*Combo Compounds (FI, RN) and Lung Cancer (FI, CT)*

=> b drugu biosis

FILE 'DRUGU' ENTERED AT 13:39:30 ON 15 JAN 2004  
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FILE 'BIOSIS' ENTERED AT 13:39:30 ON 15 JAN 2004  
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=> d que 173

```

L7      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHOTHECENE/CN
L8      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHODERMIN/CN
L9      2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L7 OR L8)
L70     2584 SEA TRICHOTHEC!NE# OR T-2 (W) TOXIN OR TRICHODERMIN# OR (NSC
(W) 267033 OR 73846) OR WG (W) 696
L71     893 SEA L9
L72     178425 SEA (CANCER? OR MALIGN? OR NEOPLAS? OR TUMOR? OR TUMOUR? OR
CARCINO? OR ADENO? OR SARCOMA?) AND (LUNG# OR PULMON?)
L73     8 SEA (L70 OR L71) AND L72

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*Combo of Compounds (RN, FI) AND Lung Cancer (FI)*

=> b wpids

FILE 'WPIDS' ENTERED AT 13:39:39 ON 15 JAN 2004  
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FILE LAST UPDATED: 12 JAN 2004 <20040112/UP>  
MOST RECENT DERWENT UPDATE: 200403 <200403/DW>  
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,

PLEASE VISIT:

[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE  
<http://thomsonderwent.com/coverage/latestupdates/> <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER  
GUIDES, PLEASE VISIT:  
<http://thomsonderwent.com/support/userguides/> <<<

>>> ADDITIONAL POLYMER INDEXING CODES WILL BE IMPLEMENTED FROM  
DERWENT UPDATE 200403.  
THE TIME RANGE CODE WILL ALSO CHANGE FROM 018 TO 2004.  
SDIS USING THE TIME RANGE CODE WILL NEED TO BE UPDATED.  
FOR FURTHER DETAILS: <http://thomsonderwent.com/chem/polymers/> <<<

=> d que 176

L74 77 SEA FILE=WPIDS ABB=ON PLU=ON (TRICHOTHEC!NE# OR T-2 (W)  
TOXIN OR TRICHODERMIN# OR (NSC (W) 267033 OR 73846) OR WG (W)  
696)/BIX  
L75 14026 SEA FILE=WPIDS ABB=ON PLU=ON (CANCER? OR MALIGN? OR NEOPLAS?  
OR TUMOR? OR TUMOUR? OR CARCINO? OR ADENO? OR SARCOMA?)/BIX  
AND (LUNG# OR PULMON?)/BIX  
L76 0 SEA FILE=WPIDS ABB=ON PLU=ON L74 AND L75

*Combo of Compounds (FT) AND Lung Cancer (FT)*

=> => dup rem 139 137 146 169 173 176

L76 HAS NO ANSWERS

PROCESSING COMPLETED FOR L39

PROCESSING COMPLETED FOR L37

PROCESSING COMPLETED FOR L46

PROCESSING COMPLETED FOR L69

PROCESSING COMPLETED FOR L73

PROCESSING COMPLETED FOR L76

L78 15 DUP REM L39 L37 L46 L69 L73 L76 (4 DUPLICATES REMOVED)  
ANSWERS '1-4' FROM FILE CAPLUS  
ANSWER '5' FROM FILE USPATFULL  
ANSWER '6' FROM FILE CANCERLIT  
ANSWERS '7-9' FROM FILE EMBASE  
ANSWERS '10-12' FROM FILE DRUGU  
ANSWERS '13-15' FROM FILE BIOSIS

=> => d ibib abs hitrn 1-5;d iall 6-

YOU HAVE REQUESTED DATA FROM FILE 'USPATFULL, CAPLUS, CANCERLIT, EMBASE, DRUGU,  
BIOSIS' - CONTINUE? (Y)/N:y

L78 ANSWER 1 OF 15 ~~CAPLUS~~ CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1  
ACCESSION NUMBER: 1997:342720 CAPLUS  
DOCUMENT NUMBER: 127:64507  
TITLE: Two-step pretargeting methods using improved  
biotin-active agent conjugates  
INVENTOR(S): Reno, John M.; Theodore, Louis J.; Gustavson, Linda M.  
PATENT ASSIGNEE(S): Neorx Corporation, USA  
SOURCE: U.S., 80 pp., Cont.-in-part of U.S. Ser. No. 995,381,  
abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5630996	A	19970520	US 1993-122979	19930916
US 5283342	A	19940201	US 1992-895588	19920609
EP 1138334	A2	20011004	EP 2001-201994	19930607
EP 1138334	A3	20020403		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE

US 5911969	A	19990615	US 1994-329617	19941026
US 6287536	B1	20010911	US 1997-788339	19970127
US 2002034511	A1	20020321	US 2001-920454	20010801

PRIORITY APPLN. INFO.:

US 1992-895588	A2	19920609
US 1992-995381	B2	19921223
US 1992-995383	B2	19921223
EP 1993-915235	A3	19930607
WO 1993-US5406	A1	19930607
US 1993-122979	A3	19930916
US 1997-788339	A1	19970127

OTHER SOURCE(S): MARPAT 127:64507

AB Methods, compds., compns. and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are disclosed. In particular, methods for radio-metal labeling of biotin and for improved radiohalogenation of biotin, as well as related compds., are described. Also, clearing agents, anti-ligand-targeting moiety conjugates, target cell retention enhancing moieties and addnl. methods are discussed. The method comprises (1) administering a 1st conjugate of antibody or fragment and streptavidin and allowing time for accumulation in target tissue (tumor), and (2) subsequently administering a 2nd biotindase-resistant conjugate of biotin and DOTA derivative (chelated with radio-metal, e.g. <sup>99m</sup>Tc or <sup>186</sup>Re). Asialoorosomuroid may be used as clearing agent for maximize targeting (tumor:blood) ratio.

IT **51724-48-2D, Trichothecene**, 2-pyridinyldithio derivs.  
**51724-48-2D, Trichothecene**, N-hydroxysuccinimide derivs.

RL: RCT (Reactant); RACT (Reactant or reagent)

(two-step pretargeting methods using conjugate of antibody and streptavidin or avidin and conjugate of biotin and DOTA radioisotope complex for treating **tumor**)

L78 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 1987:613316 CAPLUS

DOCUMENT NUMBER: 107:213316

TITLE: Effects of low-level long-term oral exposure to **T-2 toxin** in CD-1 mice

AUTHOR(S): Schiefer, H. B.; Rousseaux, C. G.; Hancock, D. S.; Blakley, B. R.

CORPORATE SOURCE: Toxicol. Res. Cent., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.

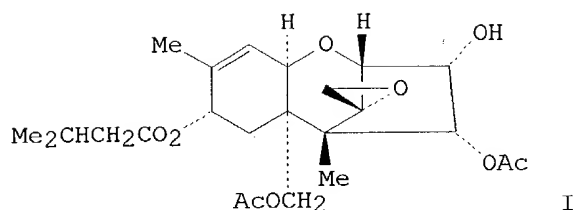
SOURCE: Food and Chemical Toxicology (1987), 25(8), 593-601  
CODEN: FCTOD7; ISSN: 0278-6915

DOCUMENT TYPE: Journal

LANGUAGE: English

GI





AB In a 16-mo feeding study, male and female mice received semisynthetic diets containing 0, 1.5, or 3.0 ppm T 2 toxin (I). Feed consumption, body-weight gains, clin. findings (including hematol. examns. at 16 mo), and the development of external lesions were recorded. At 3, 6, 12, and 16 mo, animals were killed for assessment of their immune function. Disease-related deaths did not differ among groups. Histol. examination of all organs revealed significant differences from controls in the incidence of pulmonary adenomas and hepatic adenomas in the 3.0-ppm group. Other treatment-related findings were an increased prevalence of epithelial hyperplasia in the forestomach of animals treated with, and increased heart wts. in treated male mice. T-lymphocyte-dependent humoral immunity tests did not reveal treatment effects and hematol. revealed no particular trends. Thus, chronic feeding of I at low levels is not immunosuppressive but has a carcinogenic or tumor-promoting effect in mice.

L78 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1990:133904 CAPLUS  
 DOCUMENT NUMBER: 112:133904  
 TITLE: Use of cell cultures for predicting the biological effects of mycotoxins  
 AUTHOR(S): Robbana-Barnat, Said; LaFarge-Frayssinet, Christiane; Frayssinet, Charles  
 CORPORATE SOURCE: Lab. Pathol. Cell., Inst. Rech. Sci. Cancer, Villejuif, 94802, Fr.  
 SOURCE: Cell Biology and Toxicology (1989), 5(2), 217-26  
 CODEN: CBTOE2; ISSN: 0742-2091  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB A system is described for toxicol. anal. of mycotoxins using cell cultures of different origins. The response of several cell types to 14 mycotoxins was obtained in 3 days. This approach allowed us to: demonstrate and quantify a toxic effect, define some organ specificity related to the preferential action on a particular cell type, and detect an immunosuppressive effect. The system can be used for toxicol. screening; it also has a predictive value for the pathol. effects of tested products.

IT **4682-50-2, Trichodermin**

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (immunosuppression activity and toxicity of, in animal cell cultures, organs specificity in relation to)

L78 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1985:466155 CAPLUS  
 DOCUMENT NUMBER: 103:66155  
 TITLE: A gas chromatographic procedure for the toxicological determination of **trichothecenes** in human tissues and body fluids

AUTHOR(S): Heyndrickx, A.; Sookvanichsilp, N.; Van den Heede, M.  
 CORPORATE SOURCE: Dep. Toxicol., State Univ. Ghent, Ghent, 9000, Belg.  
 SOURCE: Archives Belges de Medecine Sociale, Hygiene, Medecine  
 du Travail et Medecine Legale (1984),  
 Suppl.(Proc.-World Congr. "New Compd. Biol. Chem.  
 Warf.: Toxicol. Eval., 1st, 1984), 132-42  
 CODEN: ABMHAM; ISSN: 0003-9578

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Postmortem human tissues and body fluids, which were collected from 2 Iranian soldiers, were analyzed for trichothecene mycotoxins, because of their reported use in chemical warfare. The samples were extracted with acetonitrile, Me<sub>2</sub>CO, CHCl<sub>3</sub>, or EtOAc, and according to the nature of the sample a further purification had to be performed by washing the exts. with n-hexane or by reextg. with CHCl<sub>3</sub>. The XAD-2 resin was chosen for the final clean-up of all exts. The purified exts. were analyzed by gas chromatog. with electron capture detection. None of the sample chromatograms exhibited peaks corresponding to those of the trichothecene stds.

IT 51724-48-2D, derivs.  
 RL: BIOL (Biological study)  
 (mycotoxins, determination of, in human tissues and body fluids by gas chromatog.)

L78 ANSWER 5 OF 15 USPATFULL on STN

ACCESSION NUMBER: 2003:187405 USPATFULL  
 TITLE: Pretargeting methods and compounds  
 INVENTOR(S): Theodore, Louis J., Lynnwood, WA, UNITED STATES  
 Axworthy, Donald B., Brier, WA, UNITED STATES  
 Reno, John M., Brier, WA, UNITED STATES  
 PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, UNITED STATES, 98119  
 (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003129191	A1	20030710
APPLICATION INFO.:	US 2002-125788	A1	20020417 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2000-561736, filed on 25 Apr 2000, GRANTED, Pat. No. US 6416738 Continuation of Ser. No. US 1994-350551, filed on 7 Dec 1994, GRANTED, Pat. No. US 6075010 Continuation-in-part of Ser. No. US 1993-163184, filed on 7 Dec 1993, ABANDONED Continuation-in-part of Ser. No. WO 1993-US5406, filed on 7 Jun 1993, PENDING Continuation-in-part of Ser. No. US 1992-995381, filed on 23 Dec 1992, ABANDONED		

DOCUMENT TYPE: Utility  
 FILE SEGMENT: APPLICATION  
 LEGAL REPRESENTATIVE: SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, SEATTLE, WA, 98104-7092

NUMBER OF CLAIMS: 48  
 EXEMPLARY CLAIM: 1  
 NUMBER OF DRAWINGS: 20 Drawing Page(s)  
 LINE COUNT: 5470  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods, compounds, compositions and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are disclosed. In particular, methods for radiometal labeling of biotin, as well as related compounds, are described. Clearing agents and clearance

mechanisms are also discussed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

YOU HAVE REQUESTED DATA FROM FILE 'USPATFULL, CAPLUS, CANCERLIT, EMBASE, DRUGU, BIOSIS' - CONTINUE? (Y)/N:y

YOU HAVE REQUESTED DATA FROM 10 ANSWERS - CONTINUE? Y/(N):y

L78 ANSWER 6 OF 15 CANCERLIT on STN

ACCESSION NUMBER: 84130001 CANCERLIT

DOCUMENT NUMBER: 84130001 PubMed ID: 6697331

TITLE: Anguidine: a broad phase II study of the Southeastern Cancer Study Group.

AUTHOR: Adler S S; Lowenbraun S; Birch B; Jarrell R; Garrard J

CONTRACT NUMBER: CA-03013 (NCI)

CA-03177 (NCI)

CA-29456 (NCI)

+

SOURCE: CANCER TREATMENT REPORTS, (1984 Feb) 68 (2) 423-5.

Journal code: 7607107. ISSN: 0361-5960.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: MEDLINE; Priority Journals

OTHER SOURCE: MEDLINE 84130001

ENTRY MONTH: 198404

ENTRY DATE: Entered STN: 19941107

Last Updated on STN: 19941107

ABSTRACT:

Anguidine, a phase II agent, was used to treat 276 patients with solid tumors. The overall evaluability rate was 68%. Hematologic toxicity was substantial but not prohibitive. There were no complete responses, two partial responses, and 12 stabilizations.

CONTROLLED TERM: Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

\*Adenocarcinoma: DT, drug therapy

Breast Neoplasms: DT, drug therapy

Drug Evaluation

Head and Neck Neoplasms: DT, drug therapy

Hematologic Diseases: CI, chemically induced

Kidney Neoplasms: DT, drug therapy

Leukocyte Count

**Lung Neoplasms: DT, drug therapy**

Melanoma: DT, drug therapy

Platelet Count

\*Sesquiterpenes: TU, therapeutic use

**Trichothecenes: AE, adverse effects**

**\*Trichothecenes: TU, therapeutic use**

CAS REGISTRY NO.: 2270-40-8 (diacetoxyscirpenol)

CHEMICAL NAME: 0 (Sesquiterpenes); 0 (**Trichothecenes**)

L78 ANSWER 7 OF 15 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 3

ACCESSION NUMBER: 81031287 EMBASE  
 DOCUMENT NUMBER: 1981031287  
 TITLE: Low **tumor** incidence in rats with long-term feeding of fusarenon-X, a cytotoxic **trichothecene** produced by *Fusarium nivale*.  
 AUTHOR: Saito M.; Horiuchi T.; Ohtsubo K.; et al.  
 CORPORATE SOURCE: Dept. Carcinogenes. Cancer Susceptibility, Inst. Med. Sci., Univ. Tokyo, Japan  
 SOURCE: Japanese Journal of Experimental Medicine, (1980) 50/4 (293-302).  
 CODEN: JJEMAG  
 COUNTRY: Japan  
 DOCUMENT TYPE: Journal  
 FILE SEGMENT: 037 Drug Literature Index  
 030 Pharmacology  
 016 Cancer  
 LANGUAGE: English

## ABSTRACT:

In order to examine **tumorigenic** effects of fusarenon-X, a **\*\*\*trichothecene\*\*\*** compound produced by *Fusarium nivale*, feeding experiments on 151 male Donryu rats were carried out. A daily dose of 105 µg (7 ppm in the diet) or 50 µg (3.5 ppm)/animal of fusarenon-X was given for 1 or 2 years. Although the animals of the experimental groups showed lower body weight than controls and were more liable to be afflicted by **pulmonary** infections, **tumor** incidences were as low as that of the control group. However, several unusual **tumors** were observed only in the experimental groups: 1 **adenocarcinoma** of the stomach, 2 papillary **\*\*\*carcinomas\*\*\*** of the urinary bladder, 1 adrenocortical **adenoma**, and 1 leukemia.

CONTROLLED TERM: Medical Descriptors:  
 \***carcinogenesis**  
 \*diet  
 \*fusarium  
 adrenal cortex adenoma  
 adrenal cortex carcinoma  
 bladder carcinoma  
 dose response  
 leukemia  
 stomach carcinoma  
 bladder  
 endocrine system  
 drug response  
 animal experiment  
 oral drug administration  
 stomach  
 rat  
 Drug Descriptors:  
 \*fusarenon x  
 (fusarenon x) 23255-69-8

*Structure*  
*Shown after bibliographic hits*

CAS REGISTRY NO.:

L78 ANSWER 8 OF 15 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN

ACCESSION NUMBER: 1999073194 EMBASE  
 TITLE: Fumonisin and neural tube defects in South Texas.  
 AUTHOR: Hendricks K.  
 CORPORATE SOURCE: K. Hendricks, Infect. Dis. Epidemiol./Surveillance, Texas Department of Health, 1100 West 49th Street, Austin, TX

SOURCE: 78756, United States  
 Epidemiology, (1999) 10/2 (198-200).  
 Refs: 25  
 ISSN: 1044-3983 CODEN: EPIDEX  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; (Short Survey)  
 FILE SEGMENT: 004 Microbiology  
 008 Neurology and Neurosurgery  
 017 Public Health, Social Medicine and Epidemiology  
 052 Toxicology  
 LANGUAGE: English  
 CONTROLLED TERM: Medical Descriptors:  
 \*neural tube defect: EP, epidemiology  
 United States  
 fusarium moniliforme  
 animal food  
 corn  
 risk factor  
 encephalomalacia  
 lung edema  
 liver toxicity  
 carcinogenicity  
 hematocrit  
 food and drug administration  
 human  
 nonhuman  
 short survey  
 priority journal  
 Drug Descriptors:  
 \*fumonisin b1: TO, drug toxicity  
 zearalenone: TO, drug toxicity  
 sphingolipid: EC, endogenous compound  
 mycotoxin: TO, drug toxicity  
 folic acid  
 receptor: EC, endogenous compound  
 cholesterol: EC, endogenous compound  
 sphingosine derivative  
 synthetase  
 ceramide derivative  
 growth factor receptor: EC, endogenous compound  
 tumor necrosis factor: EC, endogenous compound  
 interleukin 1: EC, endogenous compound  
 nerve growth factor: EC, endogenous compound  
 citrinin: TO, drug toxicity  
 cyclopiazonic acid: TO, drug toxicity  
 ochratoxin: TO, drug toxicity  
 patulin: TO, drug toxicity  
 penicillic acid: TO, drug toxicity  
 sterigmatocystin: TO, drug toxicity  
 trichothecene derivative: TO, drug toxicity  
 CAS REGISTRY NO.: (fumonisin b1) 116355-83-0; (zearalenone) 17924-92-4;  
 (folic acid) 59-30-3, 6484-89-5; (cholesterol) 57-88-5;  
 (synthetase) 9031-56-5, 9031-57-6; (nerve growth factor)  
 9061-61-4; (citrinin) 11118-72-2, 518-75-2; (cyclopiazonic  
 acid) 18172-33-3, 83136-88-3; (ochratoxin) 303-47-9,  
 37203-43-3; (patulin) 149-29-1; (penicillic acid) 90-65-3;  
 (sterigmatocystin) 10048-13-2

L78 ANSWER 9 OF 15 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 79160009 EMBASE  
DOCUMENT NUMBER: 1979160009  
TITLE: Toxicity of Aspergillus and Fusarium species isolated from  
forage and bronchial aspirates of patients suffering from  
bronchial **cancer**.  
AUTHOR: Caretta G.; Del Frate G.; Picco A.M.; et al.  
CORPORATE SOURCE: Cent. Micol. Med. R. Ciferri e P. Redaelli, Univ. Pavia,  
Pavia, Italy  
SOURCE: Microbiologica, (1978) VOL.1/- (57-65).  
CODEN: MIBLDR  
COUNTRY: Italy  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 037 Drug Literature Index.  
016 Cancer  
004 Microbiology  
030 Pharmacology  
015 Chest Diseases, Thoracic Surgery and Tuberculosis  
011 Otorhinolaryngology  
LANGUAGE: English

ABSTRACT:  
255 strains, 113 of which Aspergillus and 142 Fusarium, were tested for their  
ability to elaborate mycotoxins in laboratory culture. Toxigenic species of the  
genus Aspergillus were: A. flavus (6 strains) and A. fumigatus (3 strains). All  
A. fumigatus strains and 3 A. flavus strains were isolated from bronchial  
aspirates of patients suffering from bronchial **cancer**. The isolates  
of A. flavus produced aflatoxins B1 and B1+B2; the isolates of A. fumigatus  
produced aflatoxins B2+G1, G2 and G1. The other strains of A. flavus were  
isolated from forage, peanut flour and sputum, respectively. We have isolated  
species of the genus Fusarium from forage (F. culmorum and F. equiseti), soil  
(F. moniliforme and F. oxysporum) and air (F. roseum var. gibbosum). The toxins  
elaborated by these strains were **trichothecenes**, T-  
\*\*\*2\*\*\* **toxin** and diacetoxyscirpenol, and zearalenone. Studies  
performed on the effects of different herbicides and fungicides on the  
production of aflatoxin B1 by a strain of A. flavus, showed that growth of A.  
flavus in the presence of Diuron (DMU) and Pyrazon (PCA) yielded significant  
aflatoxin B1 levels.

CONTROLLED TERM: Medical Descriptors:  
\*aspergillus  
\*alicap  
\*fusarium  
\*lenacil  
\*lung cancer  
\*metham sodium  
clinical study  
ecology  
higher plant  
in vitro study  
animal experiment  
fungus  
respiratory system  
major clinical study  
cytology  
Drug Descriptors:  
\*aflatoxin

\*dacthal  
 \*dinoseb  
 \*diuron  
 \*zineb  
 \*nortriptyline  
 \*phenmedipham  
 \*phenylbutazone  
 tiezene  
 chloridazon  
 metham sodium  
 aretil  
 lenacil  
 alicap  
 unclassified drug  
 CAS REGISTRY NO.: (aflatoxin) 1402-68-2; (dacthal) 1861-32-1; (dinoseb)  
 88-85-7; (diuron) 330-54-1; (zineb) 12122-67-7;  
 (nortriptyline) 72-69-5, 894-71-3; (phenmedipham)  
 13684-63-4; (phenylbutazone) 129-18-0, 50-33-9, 8054-70-4;  
 (chloridazon) 1698-60-8; (metham sodium) 137-42-8;  
 (lenacil) 2164-08-1  
 CHEMICAL NAME: Tiezene; Pyramin; Vapam; Karmex; Betanal; Dacthal; Aretil;  
 Venzar; Alicap

L78 ANSWER 10 OF 15 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN  
 ACCESSION NUMBER: 2003-42595 DRUGU C P  
 TITLE: Structures and cytotoxic properties of trichoverroids and  
 their macrolide analogues produced by saltwater culture of  
 Myrothecium verrucaria.  
 AUTHOR: Amagata T; Rath C; Rigot J F; Tarlov N; Tenney K; Valeriote F  
 A; Crews P  
 CORPORATE SOURCE: Univ. California  
 LOCATION: Santa Cruz., Cal.; Detroit, Mich., USA  
 SOURCE: J. Med. Chem. (40, No. 20, 4342-50, 2003) 2 Fig. 3 Tab. 42 Ref.  
 CODEN: JMCMAR ISSN: 0022-2623  
 AVAIL. OF DOC.: Dept. of Chemistry and Biochemistry and Institute for Marine  
 Sciences, University of California-Santa Cruz, Santa Cruz, CA  
 95064, U.S.A. (P.C.). (e-mail: phil@chemistry.ucsc.edu).  
 LANGUAGE: English  
 DOCUMENT TYPE: Journal

## ABSTRACT:

Saltwater culture of the Hawaiian sponge-derived fungus *Myrothecium verrucaria* yielded 3 new **trichothecenes**, 3-hydroxyroridin E (1a, NSC-724381), 13'-acetyltrichoverrin B (2, NSC-720697), and miophytocen C (3, NSC-722594), and 9 known analogs (1b, NSC-720909), (4, NSC-20694), (5, NSC-20693), (6, NSC-20162), (7a, NSC-20737), (7b, NSC-20910), (8, NSC-20696), (9a, NSC-20696), and (9b, NSC-20695). All except (3) showed significant cytotoxicity vs. murine and human **tumor** cells, using anguidin (17) as standard. Structure-activity relationships were assessed: (i) all 12,13-poxy analogs were active; (ii) a 2'-OH group conferred potency; (iii) the favored stereochemistry at C6'-C13' was 6'R,13'S for (7a,b) and 6'S,13'R for (1a,b).

SECTION HEADING: C Chemistry  
 P Pharmacology

CLASSIF. CODE: 38 Structure/Activity  
 52 Chemotherapy - non-clinical

71 Medicinal Chemistry  
72 New Drugs  
73 Trial Preparations

## CONTROLLED TERM:

NSC-722594 \*RC; NSC-720909 \*RC; NSC-720694 \*RC; NSC-720693  
\*RC; NSC-720162 \*RC; NSC-720737 \*RC; NSC-720910 \*RC;  
NSC-720696 \*RC; NSC-720696 \*RC; NSC-720695 \*RC; ANGUIDIN \*RC;  
NEW \*FT; TRIAL-PREP. \*FT; ISOL. \*FT; MYROTHECIUM \*FT;  
VERRUCARIA \*FT; STRUCT.DET. \*FT; STEREOCHEM. \*FT; IN-VITRO  
\*FT; CYTOSTATIC \*FT; CYTOSTATICS \*FT; HL60-CELL \*FT;  
HCT116-CELL \*FT; A498-CELL \*FT; MDA-MB435-CELL \*FT; FUNGUS  
\*FT; TISSUE-CULTURE \*FT; LEUKEMIA \*FT; **TUMOR-CELL**  
\*FT

[01] NSC-724381 \*OC; NSC-724381 \*PH; DR0113755 \*RN; OC \*FT; PH \*FT

[02] NSC-720697 \*OC; NSC-720697 \*PH; DR0113756 \*RN; OC \*FT; PH \*FT

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

L78 ANSWER 11 OF 15 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2000-16208 DRUGU C P M

TITLE: New **trichothecenes** isolated from *Holarrhena floribunda*.

AUTHOR: Loukaci A; Kayser O; Bindseil K U; Siems K; Frevert J; Abreu P M

CORPORATE SOURCE: Univ.Lisbon-New; Univ.Berlin-Free; Analyticon

LOCATION: Caparica, Port.; Berlin; Potsdam, Ger.

SOURCE: J.Nat.Prod. (63, No. 1, 52-56, 2000) 1 Fig. 5 Tab. 36 Ref.

CODEN: JNPRDF ISSN: 0163-3864 *Support a parent*

AVAIL. OF DOC.: Departamento de Quimica, Centro de Quimica Fina e  
Biotecnologia, FCT-UNL, 2825-114 Caparica, Portugal. (P.M.A.)  
(e-mail: pma@dq.fct.unl.pt).

LANGUAGE: English

DOCUMENT TYPE: Journal

## ABSTRACT:

Bioassay-guided fractionation of an extract of *Holarrhena floribunda* stems led to the isolation of the new **trichothecenes**, 8-dihydrotrichothecinol A (1), loukacinol A (2) and loukacinol B (3), and the known compounds, trichothecolone (4), trichothecin (5), trichothecinol A (6), rosenonolactone (7), 6-beta-hydroxy rosenonolactone (8) and rosololactone (9). Compounds (1 and 6) showed significant cytotoxicity towards several human **tumor** cell lines, whereas compound (8) showed moderate and weak antileishmanial activity against extracellular and intracellular *Leishmania donovani*, respectively.

SECTION HEADING: C Chemistry  
P Pharmacology  
M Microbiology

CLASSIF. CODE: 23 Antimicrobials  
52 Chemotherapy - non-clinical  
55 Fungicides  
71 Medicinal Chemistry  
72 New Drugs

## CONTROLLED TERM:

ISOL. \*FT; HOLARRHENA \*FT; BOTANY \*FT; FLORIBUNDA \*FT;



[01] STRUCT.DET. \*FT; IN-VITRO \*FT  
 TRICHOTHECINOL-A \*OC; TRICHOTHECINOL-A \*PH; DR9700421 \*RN;  
 CYTOSTATIC \*FT; KB-CELL \*FT; SK-MEL30-CELL \*FT; MELANOMA \*FT;  
 A549-CELL \*FT; MCF7-CELL \*FT; CYTOSTATICS \*FT; TISSUE-CULTURE  
 \*FT; **CARCINOMA** \*FT; **TUMOR-CELL** \*FT;  
**ADENOCARCINOMA** \*FT; TISSUE-CULTURE \*FT; **TUMOR**  
 -CELL \*FT; OC \*FT; PH \*FT

[02] DR0018009 \*RN; NEW \*FT; CYTOSTATIC \*FT; KB-CELL \*FT;  
 SK-MEL30-CELL \*FT; MELANOMA \*FT; A549-CELL \*FT; MCF7-CELL  
 \*FT; TISSUE-CULTURE \*FT; **CARCINOMA** \*FT;  
**TUMOR-CELL** \*FT; **ADENOCARCINOMA** \*FT;

[03] TISSUE-CULTURE \*FT; **TUMOR-CELL** \*FT; OC \*FT; PH \*FT  
 HYDROXYROSENONOLACTONE-6-BETA \*OC; HYDROXYROSENONOLACTONE-6-  
 BETA \*PH; DR0018011 \*RN; LEISHMANIA \*FT; PROTOZOACIDE \*FT;  
 DONOVANI \*FT; MAJOR \*FT; INFANTUM \*FT; ENRIETTI \*FT; CYTOTOX.  
 \*FT; MACROPHAGE \*FT; PROTOZOACIDES \*FT; NEW \*FT; PROTOZOON  
 \*FT; RES \*FT; OC \*FT; PH \*FT

FIELD AVAIL.: AB; LA; CT  
 FILE SEGMENT: Literature

L78 ANSWER 12 OF 15 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN  
 ACCESSION NUMBER: 1997-39316 DRUGU P T S  
 TITLE: Monoclonal antibodies in drug targeting.  
 AUTHOR: Panchagnula R; Dey C S  
 CORPORATE SOURCE: Nat.Inst.Pharm.Ed+Res.Nagar  
 LOCATION: Punjab, India  
 SOURCE: J.Clin.Pharm.Ther. (22, No. 1, 7-19, 1997) 141 Ref.  
 CODEN: JCPTED ISSN: 0269-4727

AVAIL. OF DOC.: Department of Pharmaceutics, National Institute of  
 Pharmaceutical Education and Research (NIPER), Sector-67,  
 S.A.S. Nagar, Punjab-160 062, India.

LANGUAGE: English  
 DOCUMENT TYPE: Journal

## ABSTRACT:

The use of monoclonal antibodies in drug targeting is reviewed, with reference to their production, drug-antibody conjugates, immunotoxins, their toxicity and to the limitations of their use.

SECTION HEADING: P Pharmacology  
 T Therapeutics  
 S Adverse Effects

CLASSIF. CODE: 20 Immunological  
 35 Adverse Reactions  
 50 Biological Response Modifiers  
 51 Chemotherapy - clinical  
 65 Drug Delivery  
 69 Reviews

## CONTROLLED TERM:

**CARCINOMA** \*TR; **CARCINOMA** \*OC;  
 INTOXICATION \*TR; **NEOPLASM** \*TR; **NEOPLASM**  
 \*OC; REVIEW \*FT; LAB.ANIMAL \*FT; IN-VIVO \*FT; CASES \*FT;  
 IN-VITRO \*FT; **TUMOR-CELL** \*FT; CYTOSTATIC \*FT;  
 TISSUE-CULTURE \*FT

[01] TARGETING \*FT; MAIN-TOPIC \*FT; MONOCLONAL \*FT; ANTIBODY \*FT;

[02]

CONJUGATE \*FT; DRUG-DELIVERY \*FT; OC \*FT  
 CHLORAMBUCIL \*OC; DOXORUBICIN \*OC; ADRIAMYCIN \*OC; ADRIAMYCIN  
 \*OC; DAUNORUBICIN \*OC; METHOTREXATE \*OC; TRIAZIQUONE \*OC;  
 TRENIMON \*OC; TRENIMON \*OC; VINDESINE \*OC; MELPHALAN \*OC;  
 CISPLATIN \*OC; FLUOROURACIL \*OC; DIPHTHERIA-TOXIN \*OC;  
 PS.EXOTOXIN \*OC; RICIN \*OC; ABRIN \*OC; RICIN-A-CHAIN \*OC;  
 RICIN-B-CHAIN \*OC; CHLORAMBUCIL \*TR; DOXORUBICIN \*TR;  
 ADRIAMYCIN \*TR; ADRIAMYCIN \*TR; DAUNORUBICIN \*TR;  
 METHOTREXATE \*TR; TRIAZIQUONE \*TR; TRENIMON \*TR; TRENIMON  
 \*TR; VINDESINE \*TR; MELPHALAN \*TR; CISPLATIN \*TR;  
 FLUOROURACIL \*TR; DIPHTHERIA-TOXIN \*TR; PS.EXOTOXIN \*TR;  
 RICIN \*TR; ABRIN \*TR; RICIN-A-CHAIN \*TR; RICIN-B-CHAIN \*TR;  
 DIGOXIN \*AE; DIGITOXIN \*AE; COLCHICINE \*AE; PARAQUAT \*AE;  
 PHENCYCLIDINE \*AE; OC \*FT; TR \*FT; AE \*FT

FIELD AVAIL.: AB; LA; CT  
 FILE SEGMENT: Literature

L78 ANSWER 13 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
 ACCESSION NUMBER: 1999:217831 BIOSIS  
 DOCUMENT NUMBER: PREV199900217831  
 TITLE: A review of worldwide contamination of cereal grains and  
 animal feed with Fusarium mycotoxins.  
 AUTHOR(S): Placinta, C. M.; D'Mello, J. P. F. [Reprint author];  
 Macdonald, A. M. C.  
 CORPORATE SOURCE: Department of Biotechnology, Scottish Agricultural College,  
 West Mains Road, Edinburgh, EH9 3JG, UK  
 SOURCE: Animal Feed Science and Technology, (March 31, 1999) Vol.  
 78, No. 1-2, pp. 21-37. print.  
 CODEN: AFSTDH. ISSN: 0377-8401.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 26 May 1999  
 Last Updated on STN: 26 May 1999

ABSTRACT: From a global perspective, three classes of Fusarium mycotoxins may be considered to be of particular importance in animal health and productivity. Within the **trichothecene** group, deoxynivalenol (DON) is widely associated with feed rejection in pigs, while **T-2** **\*\*\*toxin\*\*\*** can precipitate reproductive disturbances in sows. Another group comprising zearalenone (ZEN) and its derivatives is endowed with oestrogenic properties. The third category includes the fumonisins which have been linked with specific toxicity syndromes such as equine leukoencephalomalacia (ELEM) and porcine **pulmonary** oedema. Many toxigenic species of Fusarium are also common pathogens of cereal plants, causing diseases such as head blight of wheat and barley and ear rot of maize. Consequently, when cereal plants are infected with these fungi, there is a risk that grain may become contaminated with Fusarium mycotoxins and that these may subsequently be transferred to compound feeds. The surveillance of grain and animal feed for the occurrence of Fusarium mycotoxins continues to attract worldwide attention and has been the subject of extensive investigations over recent years. For example, high incidence rates of contamination with DON and another **trichothecene**, nivalenol (NIV), have been reported in maize samples in New Zealand. In Poland, unacceptably high values (up to 927 mg/kg) for DON were recorded for maize grain and cobs. Potentially harmful levels of DON (up to 40 mg/kg) were also observed in wheat produced in Germany, Poland, Japan, New Zealand, USA, Canada and Argentina. Samples of barley grain in Norway, Japan and USA were found with DON levels of up to 71 mg/kg. In the Norwegian study oat samples were also contaminated with DON at levels ranging from 7 to 62 mg/kg grain. Abnormally high concentrations of both NIV and ZEN have been observed in some

Japanese barley samples (up to 26 and 15 mg/kg, respectively), and in maize produced in New Zealand (up to 7 and 10.5 mg/kg, respectively). Other \*\*\*trichothecenes\*\*\* such as 3-acetyl DON, diacetyoxyscirpenol (DAS), \*\*\*T\*\*\* -2 toxin and HT-2 toxin have also been found in cereals and animal feed in both temperate and tropical countries. In Uruguay all samples of maize-based animal feeds tested were positive for fumonisin B1 (FB1). However, highest FB1 values were observed in South Africa for compound feed (11 000 mug/kg), and in Thailand and China for maize (18 800 and 25 970 mug/kg, respectively). In a study of Argentinian maize, FB2 was the major fumonisin at values of up to 11 300 mug/kg. An alarming feature of several surveys is that in the tropics in particular, several *Fusarium* mycotoxins may co-occur with each other and with aflatoxin B1, an *Aspergillus* compound sharing \*\*\*carcinogenic\*\*\* properties with fumonisins. It is concluded that, although sample size has been small in a number of surveys, there is nevertheless unequivocal evidence of global contamination of cereal grains and animal feed with several **trichothecenes**, ZEN and fumonisins. Furthermore, it is clear that legislation for the control of these mycotoxins in animal feed is now overdue and that further work is required to exploit cereal genotypes that are resistant to diseases caused by toxigenic *Fusarium* phytopathogens.

CONCEPT CODE: Toxicology - General and methods 22501  
Food technology - General and methods 13502

INDEX TERMS: Major Concepts  
Foods; Toxicology

INDEX TERMS: Chemicals & Biochemicals  
deoxynivalenol: toxin; nivalenol: toxin; zearalenone: toxin; *Fusarium* mycotoxins; **T-2 toxin**

INDEX TERMS: Miscellaneous Descriptors  
animal feed: animal feed, fungal contamination; cereal grains: fungal contamination, grain product

ORGANISM: Classifier  
Fungi Imperfecti or Deuteromycetes 15500  
Super Taxa  
Fungi; Plantae  
Organism Name  
*Fusarium*  
Taxa Notes  
Fungi, Microorganisms, Nonvascular Plants, Plants

ORGANISM: Classifier  
Suidae 85740  
Super Taxa  
Artiodactyla; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
pig  
Taxa Notes  
Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates

REGISTRY NUMBER: 51481-10-8 (deoxynivalenol)  
23282-20-4 (nivalenol) *Structure shown after h.f.s.*  
17924-92-4 (zearalenone)  
21259-20-1 (**T-2 toxin**) *One type of trichothecene*

L78 ANSWER 14 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
ACCESSION NUMBER: 1987:389094 BIOSIS  
DOCUMENT NUMBER: PREV198733069234; BR33:69234  
TITLE: MYCOTOXINS IN THE AIR.  
AUTHOR(S): FLANNIGAN B [Reprint author]

CORPORATE SOURCE: DEP BREWING BIOL SCI, HERIOT-WATT UNIV, CHAMBERS ST,  
EDINBURGH EH1 1HX, UK

SOURCE: International Biodeterioration, (1987) Vol. 23, No. 2, pp.  
73-78.  
CODEN: INBIEA. ISSN: 0265-3036.

DOCUMENT TYPE: Article

FILE SEGMENT: BR

LANGUAGE: ENGLISH

ENTRY DATE: Entered STN: 12 Sep 1987  
Last Updated on STN: 12 Sep 1987

CONCEPT CODE: Biochemistry studies - General 10060  
Respiratory system - Pathology 16006  
Toxicology - Environment and industry 22506  
Neoplasms - Carcinogens and carcinogenesis 24007  
Immunology - Immunopathology, tissue immunology 34508  
Allergy 35500  
Medical and clinical microbiology - Mycology 36008  
Public health - Air, water and soil pollution 37015  
Plant physiology - Chemical constituents 51522

INDEX TERMS: Major Concepts  
Allergy (Clinical Immunology, Human Medicine, Medical  
Sciences); Clinical Endocrinology (Human Medicine,  
Medical Sciences); Infection; Oncology (Human Medicine,  
Medical Sciences); Pollution Assessment Control and  
Management; **Pulmonary** Medicine (Human  
Medicine, Medical Sciences); Toxicology

INDEX TERMS: Miscellaneous Descriptors  
REVIEW HUMAN ASPERGILLUS-FLAVUS FUSARIUM-SP  
PENICILLIUM-OXALICUM STACHYBOTRYS-ATRA  
**TRICHOTHECENE** ALLERGIC RESPIRATORY DISEASES  
**CARCINOGENS** AIR POLLUTION

ORGANISM: Classifier  
Fungi Imperfecti or Deuteromycetes 15500  
Super Taxa  
Fungi; Plantae  
Taxa Notes  
Fungi, Microorganisms, Nonvascular Plants, Plants

ORGANISM: Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates,  
Vertebrates

REGISTRY NUMBER: **51724-48-2 (TRICHOTHECENE)**

L78 ANSWER 15 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1984:210063 BIOSIS

DOCUMENT NUMBER: PREV198477043047; BA77:43047

TITLE: CYTO TOXICITY AND ABSENCE OF MUTAGENIC ACTIVITY OF VOMI  
TOXIN 4 DEOXY NIVALENOL IN A HEPATOCYTE MEDIATED MUTATION  
ASSAY WITH V-79 CHINESE HAMSTER **LUNG** CELLS.

AUTHOR(S): ROGERS C G [Reprint author]; HEROUX-METCALF C

CORPORATE SOURCE: TOXICOL RES DIV, HEALTH PROTECTION BRANCH, HEALTH AND  
WELFARE CAN, OTTAWA, K1A 0L2, CAN

SOURCE: Cancer Letters, (1983) Vol. 20, No. 1, pp. 29-36.  
CODEN: CALEDQ. ISSN: 0304-3835.

DOCUMENT TYPE: Article

FILE SEGMENT: BA  
 LANGUAGE: ENGLISH  
 ABSTRACT: Cytotoxicity and mutagenicity of vomitoxin (4-deoxynivalenol), a tricothecene mycotoxin produced on cereal grains by fungi of the genus *Fusarium*, were determined in vitro with Chinese hamster V79 cells. Cytotoxicity was shown by a reduction in colony size at 1 µg/ml (ppm); by reduction in the number and size of colonies at 2-3 µg/ml or higher; and by lethality to 80-90% of the cells at 10 µg/ml. Up to 3 µg/ml, vomitoxin was non-mutagenic to V79 cells at the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) locus, with or without hepatocyte-mediated activation; and did not significantly increase the number of 6-thioguanine-resistant mutants at marginally cytotoxic levels of 6 and 8 µg/ml (data not shown). Vomitoxin, like other 12,13-epoxytricothecenes, may become cytotoxic through inhibition of protein and /or DNA synthesis, and is likely to be non-**carcinogenic**.  
 CONCEPT CODE: Cytology - Animal 02506  
 Genetics - Animal 03506  
 Biochemistry studies - General 10060  
 Biochemistry studies - Nucleic acids, purines and pyrimidines 10062  
 Biochemistry studies - Proteins, peptides and amino acids 10064  
 Enzymes - Physiological studies 10808  
 Metabolism - Proteins, peptides and amino acids 13012  
 Metabolism - Nucleic acids, purines and pyrimidines 13014  
 Food technology - Cereal chemistry 13510  
 Digestive system - General and methods 14001  
 Respiratory system - General and methods 16001  
 Toxicology - General and methods 22501  
 Neoplasms - Carcinogens and carcinogenesis 24007  
 Medical and clinical microbiology - Mycology 36008  
 INDEX TERMS: Major Concepts  
 Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Genetics; Infection; Metabolism; Toxicology  
 INDEX TERMS: Miscellaneous Descriptors  
 CHINESE HAMSTER LUNG V-79 CELL FUSARIUM 12 13  
 EPOXY TRICOTHECENE HYPO XANTHINE GUANINE  
 PHOSPHO RIBOSYL TRANSFERASE INHIBITED PROTEIN DNA SYNTHESIS  
 ORGANISM: Classifier  
 Fungi Imperfecti or Deuteromycetes 15500  
 Super Taxa  
 Fungi; Plantae  
 Taxa Notes  
 Fungi, Microorganisms, Nonvascular Plants, Plants  
 ORGANISM: Classifier  
 Cricetidae 86310  
 Super Taxa  
 Rodentia; Mammalia; Vertebrata; Chordata; Animalia  
 Taxa Notes  
 Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates  
 REGISTRY NUMBER: 51481-10-8 (VOMITOXIN)  
 51481-10-8 (4-DEOXYNIVALENOL)  
 42814-62-0 (12 13-EPOXYTRICOTHECENE)  
 9016-12-0 (HYPOXANTHINE-GUANINE PHOSPHORIBOSYL TRANSFERASE)

=&gt; =&gt; b reg

FILE 'REGISTRY' ENTERED AT 14:27:18 ON 15 JAN 2004  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 14 JAN 2004 HIGHEST RN 637725-36-1  
DICTIONARY FILE UPDATES: 14 JAN 2004 HIGHEST RN 637725-36-1

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

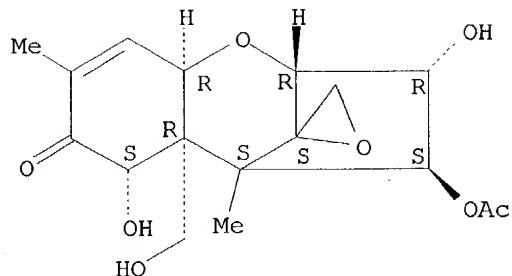
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
information enter HELP PROP at an arrow prompt in the file or refer  
to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d ide tot

L79 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 23255-69-8 REGISTRY  
CN Trichothec-9-en-8-one, 4-(acetyloxy)-12,13-epoxy-3,7,15-trihydroxy-,  
(3 $\alpha$ ,4 $\beta$ ,7 $\alpha$ )- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Spiro[2,5-methano-1-benzoxepin-10,2'-oxirane], trichothec-9-en-8-one  
deriv.  
CN Trichothec-9-en-8-one, 12,13-epoxy-3 $\alpha$ ,4 $\beta$ ,7 $\alpha$ ,15-  
tetrahydroxy-, 4-acetate (8CI)  
OTHER NAMES:  
CN 3-Acetylnivalenol  
CN 4-Acetylnivalenol  
CN 4 $\beta$ -Acetoxy-3 $\alpha$ ,7 $\alpha$ ,15-trihydroxy-12,13-epoxytrichothec-9-en-  
8-one  
CN Fusarenon X  
CN Fusarenone  
CN Fusarenone X  
CN Nivalenol monoacetate  
CN NSC 197211  
FS STEREOSEARCH  
DR 23255-72-3, 26153-10-6, 27552-17-6, 28392-39-4, 32204-36-7, 115889-63-9  
MF C17 H22 O8  
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, CHEMLIST, CSCHEM, CSNB,  
DDFU, DRUGU, EMBASE, ~~MSDB~~\*, MEDLINE, NAPRALERT, NIOSHTIC, RTECS\*,  
SPECINFO, TOXCENTER, USPAT2, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

314 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 316 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L79 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN

RN **21259-20-1** REGISTRY

CN Trichothec-9-ene-3,4,8,15-tetrol, 12,13-epoxy-, 4,15-diacetate  
 8-(3-methylbutanoate), (3 $\alpha$ ,4 $\beta$ ,8 $\alpha$ )- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Spiro[2,5-methano-1-benzoxepin-10,2'-oxirane], trichothec-9-ene-3,4,8,15-tetrol deriv.

CN Trichothec-9-ene-3 $\alpha$ ,4 $\beta$ ,8 $\alpha$ ,15-tetrol, 12,13-epoxy-,  
 4,15-diacetate 8-isovalerate (8CI)

OTHER NAMES:

CN 4 $\beta$ ,15-Diacetoxy-8 $\alpha$ -(3-methylbutyryloxy)-12,13-epoxytrichothec-9-en-3 $\alpha$ -ol

CN 8 $\alpha$ -(3-Methylbutyryloxy)-4 $\beta$ ,15-diacetoxyscirp-9-en-3 $\alpha$ -ol

CN Fusariotoxin T 2

CN Insariotoxin

CN Mycotoxin T 2

CN NSC 138780

CN T 2

CN T 2 mycotoxin

CN T 2 Toxin

CN Toxin T 2

FS STEREOSEARCH

DR 9061-58-9, 11051-21-1, 60119-99-5, 25152-34-5, 22916-10-5, 22916-18-3,  
 36653-66-4, 145427-93-6, 26400-47-5, 27640-92-2, 116163-69-0

MF C24 H34 O9

CI COM

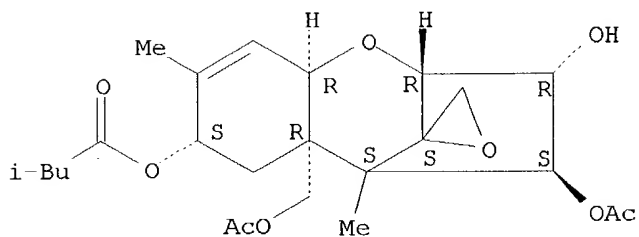
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
 BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMLIST,  
 CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB\*, IFICDB, IFIPAT, IFIUDB,  
 MEDLINE, MRCK\*, NAPRALERT, NIOSHTIC, PROMT, RTECS\*, SPECINFO, TOXCENTER,  
 USPAT2, USPATFULL, VETU

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1542 REFERENCES IN FILE CA (1907 TO DATE)

60 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1544 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> b home

FILE 'HOME' ENTERED AT 14:27:29 ON 15 JAN 2004

=>



=> b cap

FILE 'CAPLUS' ENTERED AT 15:47:23 ON 15 JAN 2004  
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FILE COVERS 1907 - 15 Jan 2004 VOL 140 ISS 3  
FILE LAST UPDATED: 14 Jan 2004 (20040114/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que 191

L7 1 SEA FILE=REGISTRY ABB=ON PLU=ON TRICHOTHECENE/CN  
L8 1 SEA FILE=REGISTRY ABB=ON PLU=ON TRICHODERMIN/CN  
L9 2 SEA FILE=REGISTRY ABB=ON PLU=ON (L7 OR L8)  
L10 293 SEA FILE=CAPLUS ABB=ON PLU=ON L9  
L32 2241 SEA FILE=CAPLUS ABB=ON PLU=ON TRICHOTHEC!NE#/OBI OR TRICHODER  
MIN#/OBI OR T-2/OBI (W) TOXIN/OBI OR (NSC/OBI (W) 267033/OBI  
OR 73846/OBI) OR WG/OBI (W) 696/OBI  
L82 67821 SEA FILE=CAPLUS ABB=ON PLU=ON (PROTEIN#/OBI OR POLYPEPTID?/OB  
I) (W) (SYNTHET?/OBI OR FORM?/OBI OR COUPL?/OBI)  
L87 7355 SEA FILE=CAPLUS ABB=ON PLU=ON (INHIBIT?/OBI OR BLOCK?/OBI)  
(L) L82  
L88 47 SEA FILE=CAPLUS ABB=ON PLU=ON (L10 OR L32) AND L87  
L91 1 SEA FILE=CAPLUS ABB=ON PLU=ON L88 AND REVIEW/DT

*Combu of Compounds (FT, RN) and Protei inhibition of Protein synthesis*

=> b uspatfull

FILE 'USPATFULL' ENTERED AT 15:47:41 ON 15 JAN 2004  
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 15 Jan 2004 (20040115/PD)  
FILE LAST UPDATED: 15 Jan 2004 (20040115/ED)  
HIGHEST GRANTED PATENT NUMBER: US6678893  
HIGHEST APPLICATION PUBLICATION NUMBER: US2004010831  
CA INDEXING IS CURRENT THROUGH 15 Jan 2004 (20040115/UPCA)  
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 15 Jan 2004 (20040115/PD)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2003  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2003

>>> USPAT2 is now available. USPATFULL contains full text of the <<<  
>>> original, i.e., the earliest published granted patents or <<<  
>>> applications. USPAT2 contains full text of the latest US <<<  
>>> publications, starting in 2001, for the inventions covered in <<<

```
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<
```

```
>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 1109

```
L7      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHOTHECENE/CN
L8      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHODERMIN/CN
L9      2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L7 OR L8)
L20     19 SEA FILE=USPATFULL ABB=ON  PLU=ON  L9
L34     78 SEA FILE=USPATFULL ABB=ON  PLU=ON  (TRICHOTHEC!NE# OR TRICHODER
      MIN# OR T-2 (W) TOXIN OR (NSC (W) 267033 OR 73846) OR WG (W)
      696)/TI,IT,AB,CLM
L107    13612 SEA FILE=USPATFULL ABB=ON  PLU=ON  (PROTEIN# OR POLYPEPTID?)/TI
      ,IT,AB,CLM (5A) (SYNTHET? OR FORM? OR COUPL?)/TI,IT,AB,CLM
L108    708 SEA FILE=USPATFULL ABB=ON  PLU=ON  (INHIBIT? OR BLOCK?)/TI,IT,A
      B,CLM (5A) L107
L109    0 SEA FILE=USPATFULL ABB=ON  PLU=ON  L108 AND (L34 OR L20)
```

COMBO OF COMPOUNDS (CF, RN) AND PROTEIN SYNTH. INHIB.

=> b medline cancerlit

FILE 'MEDLINE' ENTERED AT 15:47:57 ON 15 JAN 2004

FILE 'CANCERLIT' ENTERED AT 15:47:57 ON 15 JAN 2004

=> d que 1113

```
L7      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHOTHECENE/CN
L8      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHODERMIN/CN
L9      2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L7 OR L8)
L40     52 SEA FILE=MEDLINE ABB=ON  PLU=ON  L9
L41     1956 SEA FILE=MEDLINE ABB=ON  PLU=ON  TRICHOTHEC!NE# OR TRICHODERMIN
      # OR T-2 (W) TOXIN OR (NSC (W) 267033 OR 73846) OR WG (W) 696
L42     1724 SEA FILE=MEDLINE ABB=ON  PLU=ON  TRICHOTHECENES+NT/CT
L110    6634 SEA PROTEIN SYNTHESIS INHIBITORS/CT
L111    28 SEA (L40 OR L41 OR L42) AND L110
L113    1 SEA L111 AND REVIEW/DT
```

COMBO OF COMPOUNDS (CF, RN) AND PROTEIN SYN. INHIB

=> b embase

FILE 'EMBASE' ENTERED AT 15:48:14 ON 15 JAN 2004

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FILE COVERS 1974 TO 5 Jan 2004 (20040105/ED)

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=> d que 1115

```
L7      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHOTHECENE/CN
L8      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRICHODERMIN/CN
L9      2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L7 OR L8)
L62     432 SEA FILE=EMBASE ABB=ON  PLU=ON  L9
L64     1415 SEA FILE=EMBASE ABB=ON  PLU=ON  TRICHOTHEC!NE# OR T-2 (W)
        TOXIN OR TRICHODERMIN# OR (NSC (W) 267033 OR 73846) OR WG (W)
        696
L114    3933 SEA FILE=EMBASE ABB=ON  PLU=ON  PROTEIN SYNTHESIS INHIBITION/CT
L115    14 SEA FILE=EMBASE ABB=ON  PLU=ON  (L62 OR L64) AND L114
```

*Combo of Compounds and Protein syn. inhib.  
(F7, R9)*

=> b wpids

FILE 'WPIDS' ENTERED AT 15:48:28 ON 15 JAN 2004  
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FILE LAST UPDATED: 15 JAN 2004 <20040115/UP>  
MOST RECENT DERWENT UPDATE: 200404 <200404/DW>  
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,  
PLEASE VISIT:  
[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE  
<http://thomsonderwent.com/coverage/latestupdates/> <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER  
GUIDES, PLEASE VISIT:  
<http://thomsonderwent.com/support/userguides/> <<<

>>> ADDITIONAL POLYMER INDEXING CODES WILL BE IMPLEMENTED FROM  
DERWENT UPDATE 200403.  
THE TIME RANGE CODE WILL ALSO CHANGE FROM 018 TO 2004.  
SDIS USING THE TIME RANGE CODE WILL NEED TO BE UPDATED.  
FOR FURTHER DETAILS: <http://thomsonderwent.com/chem/polymers/> <<<

=> d que 1106

```
L74      77 SEA FILE=WPIDS ABB=ON  PLU=ON  (TRICHOTHEC!NE# OR T-2 (W)
        TOXIN OR TRICHODERMIN# OR (NSC (W) 267033 OR 73846) OR WG (W)
        696)/BIX
L104     16351 SEA FILE=WPIDS ABB=ON  PLU=ON  (PROTEIN# OR POLYPEPTID?)/BIX
        (5A) (SYNTHET? OR FORM? OR COUPL?)/BIX
L105     771 SEA FILE=WPIDS ABB=ON  PLU=ON  (INHIBIT? OR BLOCK?) (5A) L104
L106     0 SEA FILE=WPIDS ABB=ON  PLU=ON  L105 AND L74
```

*Combo of Compounds and Protein Syn. inhib.  
(F7, R9)*

=> dup rem l91 l109 l113 l115 l106

L109 HAS NO ANSWERS

L106 HAS NO ANSWERS

FILE 'CAPLUS' ENTERED AT 15:49:02 ON 15 JAN 2004

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FILE 'EMBASE' ENTERED AT 15:49:02 ON 15 JAN 2004

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PROCESSING COMPLETED FOR L91

PROCESSING COMPLETED FOR L109

PROCESSING COMPLETED FOR L113

PROCESSING COMPLETED FOR L115

PROCESSING COMPLETED FOR L106

L117 16 DUP REM L91 L109 L113 L115 L106 (0 DUPLICATES REMOVED)

ANSWER '1' FROM FILE CAPLUS

ANSWER '2' FROM FILE MEDLINE

ANSWERS '3-16' FROM FILE EMBASE

=> d ibib abs hitrn 1;d iall 2- OTHER DATABASES

L117 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1978:146814 CAPLUS

DOCUMENT NUMBER: 88:146814

TITLE: Inhibition of protein synthesis by

**trichothecenes**

AUTHOR(S): McLaughlin, Calvin S.; Vaughan, Maurice H.; Campbell, Iain M.; Wei, Cha Mer; Stafford, Mary E.; Hansen, B. S.

CORPORATE SOURCE: Dep. Mol. Biol. Biochem., Univ. California, Irvine, CA, USA

SOURCE: Mycotoxins Hum. Anim. Health, Proc. Conf. (1977), Meeting Date 1976, 263-73. Editor(s): Rodricks, Joseph V.; Hesseltine, Clifford W.; Mehlman, Myron A. Pathotox Publ., Inc.: Park Forest South, Ill. CODEN: 37OYAU

DOCUMENT TYPE: Conference; **General Review**

LANGUAGE: English

AB A review with 25 refs. on protein synthesis inhibition by trichothecene mycotoxins.

IT **51724-48-2D**, derivative

RL: BIOL (Biological study)

(**protein formation inhibition** by)

YOU HAVE REQUESTED DATA FROM 15 ANSWERS - CONTINUE? Y/(N):y

L117 ANSWER 2 OF 16 MEDLINE on STN

ACCESSION NUMBER: 96217454 MEDLINE

DOCUMENT NUMBER: 96217454 PubMed ID: 8637056

TITLE: Toxicology of deoxynivalenol (vomitoxin).

AUTHOR: Rotter B A; Prelusky D B; Pestka J J

CORPORATE SOURCE: Centre for Food and Animal Research, Agriculture and

SOURCE: Agri-Food Canada, Ottawa, Ontario, Canada.  
JOURNAL OF TOXICOLOGY AND ENVIRONMENTAL HEALTH, (1996 May)  
48 (1) 1-34. Ref: 244  
Journal code: 7513622. ISSN: 0098-4108.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, ACADEMIC)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199607

ENTRY DATE: Entered STN: 19960719  
Last Updated on STN: 19960719  
Entered Medline: 19960705

## ABSTRACT:

**Trichothecene** mycotoxins are a group of structurally similar fungal metabolites that are capable of producing a wide range of toxic effects. Deoxynivalenol (DON, vomitoxin), a **trichothecene**, is prevalent worldwide in crops used for food and feed production, including in Canada and the United States. Although DON is one of the least acutely toxic **\*\*\*trichothecenes\*\*\***, it should be treated as an important food safety issue because it is a very common contaminant of grain. This review focuses on the ability of DON to induce toxicologic and immunotoxic effects in a variety of cell systems and animal species. At the cellular level, the main toxic effect is inhibition of protein synthesis via binding to the ribosome. In animals, moderate to low ingestion of toxin can cause a number of as yet poorly defined effects associated with reduced performance and immune function. The main overt effect at low dietary concentrations appears to be a reduction in food consumption (anorexia), while higher doses induce vomiting (emesis). DON is known to alter brain neurochemicals. The serotonergic system appears to play a role in mediation of the feeding behavior and emetic response. Animals fed low to moderate doses are able to recover from initial weight losses, while higher doses induce more long-term changes in feeding behavior. At low dosages of DON, hematological, clinical, and immunological changes are also transitory and decrease as compensatory/adaptation mechanisms are established. Swine are more sensitive to DON than mice, poultry, and ruminants, in part because of differences in metabolism of DON, with males being more sensitive than females. The capacity of DON to alter normal immune function has been of particular interest. There is extensive evidence that DON can be immunosuppressive or immunostimulatory, depending upon the dose and duration of exposure. While immunosuppression can be explained by the inhibition of translation, immunostimulation can be related to interference with normal regulatory mechanisms. In vivo, DON suppresses normal immune response to pathogens and simultaneously induces autoimmune-like effects which are similar to human immunoglobulin A (IgA) nephropathy. Other effects include superinduction of cytokine production by T helper cells (in vitro) and activation of macrophages and T cells to produce a proinflammatory cytokine wave that is analogous to that found in lipopolysaccharide-induced shock (in vivo). To what extent the elevation of cytokines contributes to metabolic effects such as decreased feed intake remains to be established. Although these effects have been largely characterized in the mouse, several investigations with DON suggest that immunotoxic effects are also likely in domestic animals. Further toxicology studies and an assessment of the potential of DON to be an etiologic agent in human disease are warranted.

CONTROLLED TERM: Check Tags: Animal; Human  
Absorption  
Cell Division: DE, drug effects  
Food Contamination

Guidelines

Immune System: CY, cytology

\*Immune System: DE, drug effects

Immunosuppressive Agents: TO, toxicity

Immunotoxins: TO, toxicity

Neurotoxins: TO, toxicity

**Protein Synthesis Inhibitors: TO, toxicity**

Structure-Activity Relationship

Tissue Distribution

**Trichothecenes: CH, chemistry**

**Trichothecenes: ME, metabolism**

**\*Trichothecenes: TO, toxicity**

CAS REGISTRY NO.: 51481-10-8 (deoxynivalenol)

CHEMICAL NAME: 0 (Immunosuppressive Agents); 0 (Immunotoxins); 0 (Neurotoxins); 0 (Protein Synthesis Inhibitors); 0 (**Trichothecenes**)

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ACCESSION NUMBER: 2003471083 EMBASE

TITLE: Comparative susceptibility of B cells with different lineages to cytotoxicity and apoptosis induction by translational inhibitors.

AUTHOR: Uzarski R.L.; Pestka J.J.

CORPORATE SOURCE: Dr. J.J. Pestka, 234 G.M. Trout Bldg., Dept. of Food Sci. and Hum. Nutr., Michigan State University, East Lansing, MI 48824-1224, United States. pestka@msu.edu

SOURCE: Journal of Toxicology and Environmental Health - Part A, (28 Nov 2003) 66/22 (2105-2118).

Refs: 43

ISSN: 1528-7394 CODEN: JTEHD6

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

052 Toxicology

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

The **trichothecene** mycotoxins, Shiga toxins (STs), and ricin are potent translational inhibitors that exert diverse mechanisms of action but all have the capacity to induce death by apoptosis. Germinal centers containing actively dividing B cells are particularly sensitive to protein synthesis inhibition, and, of these, the immature B cell is reportedly most susceptible to apoptosis. The objective of this study was to test the hypothesis that immature and mature B-cell lineages were differentially susceptible to apoptosis and cytotoxicity induction by representative **trichothecene** mycotoxins, ST-1, and ricin, as well as cycloheximide (CHX), a prototypical protein synthesis inhibitor commonly used to study cell signal transduction. WEHI-231 and CH31 cells were used as representatives of phenotypically immature B cells, whereas CH12.LX cells were used to model mature B cells. Resultant data suggest that Type D and Type A **trichothecenes**, ricin, and ST-1 were more potent inducers of apoptosis than CHX, whereas Type B and Type A **\*\*\*trichothecene\*\*\*** metabolites were less. CHX and the **trichothecenes** affected immature and mature B cells equally, thus suggesting that toxicity due to these natural toxins was lineage independent. In contrast, mature B cells were more sensitive to ricin- and ST-1-induced cytotoxicity and apoptosis than

immature B cells. Taken together, these results suggest that B cells are targets of a diverse array of naturally occurring translational inhibitors. Upregulation of apoptosis in B lymphocytes may contribute to the impairment of the immune response and other symptoms described following exposure to these toxins.

CONTROLLED TERM: Medical Descriptors:  
 \*apoptosis  
 \*cytotoxicity  
 \*B lymphocyte  
 \*cell lineage  
 genotoxicity  
 germinal center  
 translation regulation  
 B lymphocyte activation  
**protein synthesis inhibition**  
 upregulation  
 immunostimulation  
 immunopathology  
 nonhuman  
 mouse  
 controlled study  
 animal cell  
 article  
 priority journal  
 Drug Descriptors:  
 \*trichothecene: TO, drug toxicity  
 \*mycotoxin: TO, drug toxicity  
 \*Shiga toxin: TO, drug toxicity  
 \*ricin: TO, drug toxicity  
 \*cycloheximide: TO, drug toxicity  
 protein synthesis inhibitor: TO, drug toxicity  
 carrier protein: EC, endogenous compound  
 CAS REGISTRY NO.: (trichothecene) 51724-48-2; (Shiga toxin) 75757-64-1; (ricin) 9009-86-3; (cycloheximide) 642-81-9, 66-81-9; (carrier protein) 80700-39-6

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ACCESSION NUMBER: 2003199451 EMBASE  
 TITLE: **Trichothecenes** in the environment: Relevance to human health.  
 AUTHOR: Sudakin D.L.  
 CORPORATE SOURCE: D.L. Sudakin, Dept. of Environ./Molec. Toxicology, Oregon State University, 333 Weniger, Corvallis, OR 97331-6502, United States. sudakind@ace.orst.edu  
 SOURCE: Toxicology Letters, (20 Jul 2003) 143/2 (97-107).  
 Refs: 85  
 ISSN: 0378-4274 CODEN: TOLED5  
 COUNTRY: Ireland  
 DOCUMENT TYPE: Journal; (Short Survey)  
 FILE SEGMENT: 004 Microbiology  
 017 Public Health, Social Medicine and Epidemiology  
 025 Hematology  
 052 Toxicology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ABSTRACT:

**Trichothecenes** are agriculturally important mycotoxins of relevance to human health. Fungi capable of producing **trichothecenes** can be found throughout the world, and include certain species of *Fusarium*, *Myrothecium*, and *Stachybotrys*. The production of mycotoxins by these toxigenic species is determined by genetic factors and the environmental conditions of their growth. The environmental fate of **trichothecenes** may be affected by other microorganisms that can detoxify them. Deoxynivalenol and \*\*\*T\*\*\* -2 toxin are examples of **trichothecenes** that are detectable as natural and unavoidable contaminants of certain agricultural commodities as well as commercial foods. Current estimates of dietary exposure to deoxynivalenol and **T-2 toxin** are below thresholds for adverse effects that have been reported in experimental animal studies, although historical epidemics of human illness have rarely been described in association with consumption of food derived from heavily contaminated grains. The toxicodynamic properties of \*\*\*trichothecenes\*\*\* include inhibition of protein synthesis and immunomodulatory effects. Very little information is available relating to their toxicokinetics and toxicodynamics in humans. While there is general agreement that the diet represents an important source of human exposure to \*\*\*trichothecenes\*\*\*, risk assessment from non-dietary routes of exposure is complicated by the limited epidemiological data that are currently available.

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CONTROLLED TERM: Medical Descriptors:

- \*human impact (environment)
- \*leukopenia: EP, epidemiology
- Fusarium*
- Stachybotrys*
- genetic toxicology
- genetic variability
- environmental factor
- detoxification
- fungal detection
- agriculture
- food contamination
- organismal interaction
- epidemic
- food intake
- toxicokinetics
- protein synthesis inhibition**
- immunomodulation
- risk assessment
- health
- correlation analysis
- chemistry
- diet
- environmental impact assessment
- molecular dynamics
- seroepidemiology
- species endemicity
- gastrointestinal disease: CO, complication
- gastrointestinal disease: EP, epidemiology
- infectious complication: CO, complication
- infectious complication: EP, epidemiology
- bleeding: CO, complication
- bleeding: EP, epidemiology
- environmental exposure
- nonhuman



short survey  
priority journal  
Drug Descriptors:  
\*trichothecene derivative  
mycotoxin  
vomitoxin  
T 2 toxin

CAS REGISTRY NO.: (vomitoxin) 51481-10-8; (T 2 toxin) 21259-20-1

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ACCESSION NUMBER: 2001432339 EMBASE

TITLE: Differential upregulation of TNF- $\alpha$ , IL-6, and IL-8 production by deoxynivalenol (Vomitoxin) and other 8-ketotrichothecenes in a human macrophage model.

AUTHOR: Sugita-Konishi Y.; Pestka J.J.

CORPORATE SOURCE: Dr. J.J. Pestka, 234 G. M. Trout Building, Department of Food Science, Michigan State University, East Lansing, MI 48824-1224, United States. pestka@msu.edu

SOURCE: Journal of Toxicology and Environmental Health - Part A, (21 Dec 2001) 64/8 (619-636).  
Refs: 54

ISSN: 1528-7394 CODEN: JTEHD6

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 046 Environmental Health and Pollution Control  
052 Toxicology

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

The effects of deoxynivalenol (DON or vomitoxin) and four closely related 8-ketotrichothecenes on proinflammatory cytokine and chemokine production were evaluated in a clonal human macrophage model. U-937 cells, which represent a human monocytelike histocytic lymphoma, were differentiated into macrophages by preincubation with phorbol 12-myristate 13-acetate (PMA). Differentiated macrophages were incubated with DON in the absence or presence of lipopolysaccharide (LPS), and supernatant was analyzed by enzyme-linked immunosorbent assay (ELISA) for the proinflammatory cytokines interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and for the chemokine interleukin-8 (IL-8). In the absence of LPS, DON at 500 or 1000 ng/ml upregulated TNF- $\alpha$  production as early as 3 h and up to 6 h, whereas 100 to 1000 ng/ml of DON significantly increased production of IL-6 from 3 to 24 h and IL-8 from 6 to 48 h. In cells costimulated with 0.2  $\mu$ g/ml LPS, DON at 500 or 1000 ng/ml markedly superinduced TNF- $\alpha$  and IL-8 production. Although 100 ng/ml of DON also potentiated LPS-induced IL-6 production, 500 or 1000 ng/ml of the toxin suppressed the LPS-induced IL-6 response. Four other 8-ketotrichothecenes, fusarenon X, nivalenol, 3-acetyl DON, and 15-acetyl DON, were also capable of upregulating or suppressing TNF- $\alpha$ , IL-6, and IL-8 production at concentrations similar to that of DON. In total, the results suggest that DON and other 8-ketotrichothecenes have the potential to both directly induce and superinduce proinflammatory cytokine and chemokine expression in human macrophages, even at toxin concentrations that are cytotoxic.

CONTROLLED TERM: Medical Descriptors:  
\*receptor upregulation  
\*macrophage activation

enzyme linked immunosorbent assay  
target cell  
cell death  
concentration response  
contamination  
toxicity testing  
cell viability  
immune response

**protein synthesis inhibition**

human  
animal experiment  
animal model  
controlled study  
human cell  
article  
priority journal

**Drug Descriptors:**

\*tumor necrosis factor alpha  
\*interleukin 6  
\*interleukin 8  
\*vomitoxin  
\*8 ketotrichothecene

**trichothecene**

phorbol 12 acetate 13 myristate  
cytokine  
sesquiterpenoid  
unclassified drug

CAS REGISTRY NO.: (interleukin 8) 114308-91-7; (vomitoxin) 51481-10-8; (  
**trichothecene**) **51724-48-2**; (phorbol 12  
acetate 13 myristate) 31365-46-5

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ACCESSION NUMBER: 2002046183 EMBASE

TITLE: Preventive effect of selenium on **T-2**  
**toxin** membrane toxicity.

AUTHOR: Keshavarz S.A.; Memarbashi A.; Balali M.

CORPORATE SOURCE: S.A. Keshavarz, School of Public Health, Institute of  
Public Health Research, Tehran Univ. of Medical Sciences,  
P.O.Box 6446-14155, Tehran, Iran (Islamic Republic of)

SOURCE: Advances in Experimental Medicine and Biology, (2001) 500/-  
(463-466).

Refs: 14

ISSN: 0065-2598 CODEN: AEMBAP

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 030 Pharmacology  
037 Drug Literature Index  
052 Toxicology

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:**

**T-2 toxin**, one of the major toxic  
\*\*\*trichothecene\*\*\* mycotoxins, has been shown to cause effects such as  
inhibition of protein synthesis and impairment of mitochondrial function. The  
use of **T-2 toxin** as chemical warfare in south  
east Asia and Iran has been reported. It has been suggested that **T-**  
\*\*\*2\*\*\* **toxin** may mediate its toxic effect via the cell membrane,

but mechanism of action is poorly understood. In cytotoxicity studies, erythrocytes are an excellent model system. In the present study different doses of sodium selenite were injected into male albino mice for 6 days every 48h. Blood samples were taken from experimental and control groups ( normal saline ). The red cells were counted in isotonic phosphate buffer containing different doses of **T-2 toxin**. The mixture was incubated at 37°(c) for 4h. The results indicate that selenium is able to prevent erythrocyte membrane damage induced by **T-2** \*\*\*toxin.\*\*\* The protective effect of selenium may be due to its membrane stabilizing properties, although inhibition of lipid peroxidation is likely, too.

CONTROLLED TERM: Medical Descriptors:  
 \*cytotoxicity  
 \*antioxidant activity  
**protein synthesis inhibition**  
 mitochondrion  
 chemical warfare  
 Southeast Asia  
 Iran  
 cell membrane  
 lipid peroxidation  
 nonhuman  
 male  
 mouse  
 animal experiment  
 animal model  
 controlled study  
 animal cell  
 conference paper  
 priority journal  
 Drug Descriptors:  
 \*selenium: PD, pharmacology  
**\*T 2 toxin**  
**\*trichothecene**  
 sodium chloride

CAS REGISTRY NO.: (selenium) 7782-49-2; (**T 2 toxin**) 21259-20-1; (**trichothecene**) **51724-48-2**; (sodium chloride) 7647-14-5

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ACCESSION NUMBER: 2001059260 EMBASE  
 TITLE: Isolation, and biological properties of a new cell cycle inhibitor, curvularol, isolated from Curvularia sp. RK97-F166.  
 AUTHOR: Honda Y.; Ueki M.; Okada G.; Onose R.; Usami R.; Horikoshi K.; Osada H.  
 CORPORATE SOURCE: H. Osada, RIKEN Institute, 2-1 Hirosawa, Wako-shi, Saitama 351-0198, Japan. hisyo@postman.riken.go.jp  
 SOURCE: Journal of Antibiotics, (2001) 54/1 (10-16).  
 Refs: 17  
 ISSN: 0021-8820 CODEN: JANTAJ  
 COUNTRY: Japan  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 004 Microbiology  
 016 Cancer  
 030 Pharmacology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

## ABSTRACT:

A new cell growth inhibitor, curvularol, was isolated from the fermentation broth of *Curvularia* sp. RK97-F166. Curvularol showed no antibacterial activity, and very weak antifungal activity. However, curvularol inhibited the cell cycle progression of normal rat kidney (NRK) cells in G(1) phase at 150 ng/ml. Curvularol induced the morphological reversion of src(ts)-transformed NRK cells at 100 ng/ml, and inhibited protein synthesis same as cycloheximide.

## CONTROLLED TERM:

Medical Descriptors:

\**Curvularia*  
 drug isolation  
 fermentation  
 antibacterial activity  
 antifungal activity  
 cell cycle G1 phase  
 kidney cell  
 virus cell transformation  
 Rous sarcoma oncovirus  
 virus mutant  
 cell structure  
 concentration response

**protein synthesis inhibition**

cytotoxicity  
 minimum inhibitory concentration  
 drug purification  
 drug structure  
 IC 50  
 human  
 nonhuman  
 rat  
 controlled study  
 human cell  
 animal cell  
 article  
 priority journal  
 Drug Descriptors:  
 \*curvularol: AN, drug analysis  
 \*curvularol: CM, drug comparison  
 \*curvularol: DV, drug development  
 \*curvularol: PD, pharmacology  
 protein synthesis inhibitor: AN, drug analysis  
 protein synthesis inhibitor: DV, drug development  
 protein synthesis inhibitor: PD, pharmacology  
 cycloheximide: CM, drug comparison  
 cycloheximide: PD, pharmacology  
 nivalenol: AN, drug analysis  
 nivalenol: CM, drug comparison  
 nivalenol: PD, pharmacology  
 verrucarol derivative: AN, drug analysis  
 verrucarol derivative: CM, drug comparison  
 verrucarol derivative: PD, pharmacology  
 t 2 toxin tetraol: AN, drug analysis  
 t 2 toxin tetraol: CM, drug comparison  
 t 2 toxin tetraol: PD, pharmacology  
 trichothecene derivative: AN, drug analysis

trichothecene derivative: CM, drug comparison  
trichothecene derivative: PD, pharmacology  
daunorubicin: CM, drug comparison  
daunorubicin: PD, pharmacology  
dactinomycin: CM, drug comparison  
dactinomycin: PD, pharmacology  
unclassified drug

CAS REGISTRY NO.: (cycloheximide) 642-81-9, 66-81-9; (nivalenol) 23282-20-4;  
(t 2 toxin tetraol)  
34114-99-3; (daunorubicin) 12707-28-7, 20830-81-3,  
23541-50-6; (dactinomycin) 1402-38-6, 1402-58-0, 50-76-0

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ACCESSION NUMBER: 2001034500 EMBASE  
TITLE: Mycotoxins and toxigenic fungi.  
AUTHOR: Pitt J.I.; Basilico J.C.; Abarca M.L.; Lopez C.  
CORPORATE SOURCE: Dr. J.I. Pitt, Food Science Australia, P.O. Box 52, North  
Ryde, NSW 2113, Australia. John.Pitt@foodscience.afisc.csir  
o.au

SOURCE: Medical Mycology, (2000) 38/SUPPL. 1 (41-46).  
Refs: 50

ISSN: 1369-3786 CODEN: MEMYFR

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 004 Microbiology  
052 Toxicology  
005 General Pathology and Pathological Anatomy  
008 Neurology and Neurosurgery  
016 Cancer  
028 Urology and Nephrology  
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:  
Mycotoxins and the fungi that produce them are of increasing importance as causes of human illness, but the diseases produced remain poorly understood at the clinical level. This paper explores four aspects: the increase of interest in ochratoxin A, factors affecting mycotoxin production, toxicology of the major mycotoxins, and the identification of *Penicillium* species which cause food spoilage and are important in indoor air.

CONTROLLED TERM: Medical Descriptors:  
human  
nonhuman  
toxicology  
*Penicillium*  
toxicokinetics  
protein synthesis  
protein analysis  
fungus identification  
food spoilage  
*Fusarium*  
*Aspergillus*  
carcinogenicity  
food contamination  
food intake  
**protein synthesis inhibition**

gastrointestinal symptom: ET, etiology  
 central nervous system disease: ET, etiology  
 immune response  
 sexual dysfunction: ET, etiology  
 isolation procedure  
 air pollutant  
 kidney disease: ET, etiology  
 conference paper  
 Drug Descriptors:

\*mycotoxin: EC, endogenous compound  
 \*mycotoxin: TO, drug toxicity  
 \*ochratoxin: EC, endogenous compound  
 \*ochratoxin: TO, drug toxicity  
 aflatoxin: EC, endogenous compound  
 aflatoxin: TO, drug toxicity  
 vomitoxin: EC, endogenous compound  
 vomitoxin: TO, drug toxicity  
 nivalenol: EC, endogenous compound  
 nivalenol: TO, drug toxicity  
 zearalenone: EC, endogenous compound  
 zearalenone: TO, drug toxicity  
 fumonisin B1: EC, endogenous compound  
 fumonisin B1: TO, drug toxicity  
 aflatoxin B1: EC, endogenous compound  
 aflatoxin B1: TO, drug toxicity

**trichothecene derivative: EC, endogenous compound**

**trichothecene derivative: TO, drug toxicity**

CAS REGISTRY NO.: (ochratoxin) 303-47-9, 37203-43-3; (aflatoxin) 1402-68-2;  
 (vomitoxin) 51481-10-8; (nivalenol) 23282-20-4;  
 (zearalenone) 17924-92-4; (fumonisin B1) 116355-83-0;  
 (aflatoxin B1) 1162-65-8

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ACCESSION NUMBER: 1999172999 EMBASE

TITLE: **Trichothecene** mycotoxins trigger a ribotoxic stress response that activates c-Jun N-terminal kinase and p38 mitogen-activated protein kinase and induces apoptosis.

AUTHOR: Shifrin V.I.; Anderson P.

CORPORATE SOURCE: P. Anderson, Division of Rheumatology, Brigham and Women's Hospital, Boston, MA 02115, United States.

SOURCE: panderson@rics.bwh.harvard.edu  
 Journal of Biological Chemistry, (14 May 1999) 274/20 (13985-13992).

Refs: 57

ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
 029 Clinical Biochemistry  
 030 Pharmacology  
 037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

The **trichothecene** family of mycotoxins inhibit protein synthesis by binding to the ribosomal peptidyltransferase site. Inhibitors of the peptidyltransferase reaction (e.g. anisomycin) can trigger a ribotoxic stress

response that activates c-Jun N-terminal kinase (JNK)/p38 mitogen-activated protein kinases, components of a signaling cascade that regulates cell survival in response to stress. We have found that selected **trichothecenes** strongly activate JNK/p38 kinases and induce rapid apoptosis in Jurkat T cells. Although the ability of individual **trichothecenes** to inhibit protein synthesis and activate JNK/p38 kinases are dissociable, both effects contribute to the induction of apoptosis. Among **trichothecenes** that strongly activate JNK/p38 kinases, induction of apoptosis increases linearly with inhibition of protein synthesis. Among **trichothecenes** that strongly inhibit protein synthesis, induction of apoptosis increases linearly with activation of JNK/p38 kinases. **Trichothecenes** that inhibit protein synthesis without activating JNK/p38 kinases inhibit the function (i.e. activation of JNK/p38 kinases and induction of apoptosis) of apoptotic \*\*\*trichothecenes\*\*\* and anisomycin, Harringtonine, a structurally unrelated protein synthesis inhibitor that competes with **trichothecenes** (and anisomycin) for ribosome binding, also inhibits the activation of JNK/p38 kinases and induction of apoptosis by **trichothecenes** and anisomycin. Taken together, these results implicate the peptidyltransferase site as a regulator of both JNK/p38 kinase activation and apoptosis.

CONTROLLED TERM: Medical Descriptors:  
 \*enzyme activation  
 \*apoptosis  
 enzyme activity  
 signal transduction  
 leukemia cell line  
**protein synthesis inhibition**  
 drug mechanism  
 drug protein binding  
 human  
 human cell  
 article  
 priority journal  
 Drug Descriptors:  
**\*trichothecene: PD, pharmacology**  
 \*mycotoxin: PD, pharmacology  
 \*stress activated protein kinase: EC, endogenous compound  
 \*mitogen activated protein kinase: EC, endogenous compound  
 anisomycin  
 harringtonine  
 CAS REGISTRY NO.: (**trichothecene**) 51724-48-2; (stress activated protein kinase) 155215-87-5; (mitogen activated protein kinase) 142243-02-5; (anisomycin) 22862-76-6; (harringtonine) 26833-85-2  
 COMPANY NAME: Sigma

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ACCESSION NUMBER: 1999023046 EMBASE  
 TITLE: Highly sensitive protein translation assay for **trichothecene** toxicity in airborne particulates: Comparison with cytotoxicity assays.  
 AUTHOR: Yike I.; Allan T.; Sorenson W.G.; Dearborn D.G.  
 CORPORATE SOURCE: D.G. Dearborn, Case Western Reserve University, Department of Pediatrics, Division of Pediatric Pulmonology, 11100 Euclid Ave., Cleveland, OH 44106-6006, United States. dxd9@po.cwru.edu  
 SOURCE: Applied and Environmental Microbiology, (1999) 65/1

(88-94).

Refs: 30

ISSN: 0099-2240 CODEN: AEMIDF

COUNTRY:

United States

DOCUMENT TYPE:

Journal; Article

FILE SEGMENT:

004 Microbiology

046 Environmental Health and Pollution Control

052 Toxicology

LANGUAGE:

English

SUMMARY LANGUAGE:

English

ABSTRACT:

Screening assays for environmental mycotoxins in bulk samples currently use cytotoxicity in cell cultures, but their application to air particulate samples often lacks sensitivity and specificity for fungal spores. An assay based on inhibition of protein synthesis using translation of firefly luciferase in a rabbit reticulocyte system has been developed for the detection of

\*\*\*trichothecene\*\*\* mycotoxins found in the spores of toxigenic fungi.

Ethanol extracts of air particulates trapped on polycarbonate filters are ultrafiltered and applied at several dilutions to a translation reaction mixture. The activity of translated luciferase is measured directly in a luminometer, eliminating the need for radioisotopes and time-consuming sample processing. Parallel standard curves using a commercially available

\*\*\*trichothecene\*\*\* provide for expression of the results in T-

\*\*\*2\*\*\* toxin equivalents per cubic meter of air. The assay can be completed in 2 h and is readily applicable to multiple samples. Comparison to the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide cytotoxicity assay indicates a 400-fold increase in sensitivity of **trichothecene**

detection in addition to a much higher specificity for these toxins. Initial field testing indicates a strong correlation between the measured level of toxicity and the presence of toxigenic fungi detected with microbiological methods. In conclusion, this luciferase translation assay offers a rapid and highly sensitive and specific method for quantitative detection of

\*\*\*trichothecene\*\*\* mycotoxin activity in air particulate samples.

CONTROLLED TERM:

Medical Descriptors:

\*RNA translation

\*toxicity testing

\*air pollution

particulate matter

cytotoxicity

fungus spore

**protein synthesis inhibition**

reticulocyte

rabbit

quantitative assay

air sampling

nonhuman

controlled study

animal cell

article

Drug Descriptors:

**\*trichothecene: TO, drug toxicity**

\*mycotoxin: TO, drug toxicity

luciferase

alcohol

3 (4,5 dimethyl 2 thiazolyl) 2,5 diphenyltetrazolium

bromide

CAS REGISTRY NO.:

**(trichothecene) 51724-48-2;**



(luciferase) 61970-00-1, 9014-00-0; (alcohol) 64-17-5; (3  
(4,5 dimethyl 2 thiazolyl) 2,5 diphenyltetrazolium bromide)  
298-93-1

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ACCESSION NUMBER: 1998096704 EMBASE

TITLE: **Trichothecene** 3-O-acetyltransferase protects both  
the producing organism and transformed yeast from related  
mycotoxins. Cloning and characterization of Tril01.

AUTHOR: Kimura M.; Kaneko I.; Komiyama M.; Takatsuki A.; Koshino  
H.; Yoneyama K.; Yamaguchi I.

CORPORATE SOURCE: M. Kimura, Microbial Toxicology Laboratory, Institute of  
Physical/Chemical Res., 2-1 Hirosawa, Wako-shi, Saitama  
351-01, Japan

SOURCE: Journal of Biological Chemistry, (1998) 273/3 (1654-1661).

Refs: 40

ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

**Trichothecene** mycotoxins such as deoxynivalenol, 4,15-  
diacetoxyscirpenol, and **T-2 toxin**, are potent  
protein synthesis inhibitors for eukaryotic organisms. The 3-O-acetyl  
derivatives of these toxins were shown to reduce their in vitro activity  
significantly as assessed by assays using a rabbit reticulocyte translation  
system. The results suggested that the introduction of an O-acetyl group at the  
C-3 position in the biosynthetic pathway works as a resistance mechanism for  
*Fusarium* species that produce t- type **trichothecenes** (  
\*\*\*trichothecenes\*\*\* synthesized via the precursor trichotriol). A gene  
responsible for the 3-O-acetylation reaction, Tril01, has been successfully  
cloned from a *Fusarium graminearum* cDNA library that was designed to be  
expressed in *Schizosaccharomyces pombe*. Fission yeast transformants were  
selected for their ability to grow in the presence of **T-2**  
\*\*\*toxin\*\*\*, and this strategy allowed isolation of 25 resistant clones, all  
of which contained a cDNA for Tril01. This is the first drug-inactivating O-  
acetyltransferase gene derived from antibiotic-producing organisms. The open  
reading frame of Tril01 codes for a polypeptide of 451 amino acid residues,  
which shows no similarity to any other proteins reported so far. TRI101 from  
recombinant *Escherichia coli* catalyzes O-acetylation of the  
\*\*\*trichothecene\*\*\* ring specifically at the C-3 position in an  
acetyl-CoA-dependent manner. By using the Tril01 cDNA as a probe, two least  
overlapping cosmid clones that cover a region of 70 kilobase pairs have been  
isolated from the genome of *F. graminearum*. Other **trichothecene**  
biosynthetic genes, Tri4, Tri5, and Tri6, were not clustered in the region  
covered by these cosmid clones. These new cosmid clones are considered to be  
located in other parts of the large biosynthetic gene cluster and might be  
useful for the study of **trichothecene** biosynthesis.

CONTROLLED TERM: Medical Descriptors:  
\*molecular cloning  
\*fusarium  
\*schizosaccharomyces pombe  
dna probe  
**protein synthesis inhibition**

escherichia coli  
 cosmid  
 toxin structure  
 nonhuman  
 article  
 priority journal  
 Drug Descriptors:  
 \*mycotoxin  
 \*trichothecene  
 \*acyltransferase  
 vomitoxin  
 t 2 toxin  
 diacetoxyscirpenol

CAS REGISTRY NO.: (trichothecene) 51724-48-2;  
 (acyltransferase) 9012-30-0, 9054-54-0; (vomitoxin)  
 51481-10-8; (t 2 toxin)  
 21259-20-1; (diacetoxyscirpenol) 2270-40-8

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ACCESSION NUMBER: 1998186041 EMBASE  
 TITLE: Toxic effects of deoxynivalenol on ribosomes and tissues of  
 the spring wheat cultivars Frontana and Casavant.  
 AUTHOR: Miller J.D.; Ewen M.A.  
 CORPORATE SOURCE: J.D. Miller, Department of Chemistry, Carleton University,  
 Ottawa, Ont. K15 5B6, Canada. jdmiller@ccs.carleton.ca  
 SOURCE: Natural Toxins, (1997) 5/6 (234-237).  
 Refs: 21  
 ISSN: 1056-9014 CODEN: NATOEE  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 029 Clinical Biochemistry  
 052 Toxicology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ABSTRACT:

The toxic effects of the Fusarium graminearum trichothecene toxin  
 deoxynivalenol were determined on ribosomes and leaf tissues of the fusarium  
 head blight-resistant spring wheat cultivar Frontana and the susceptible spring  
 wheat cultivar Casavant. The use of a poly-U-directed 14C-phenylalanine and  
 deoxynivalenol ribosome-binding assays provided evidence of resistance to the  
 protein-synthesis inhibition effects of deoxynivalenol in the head  
 blight-resistant cultivar Frontana. This is probably due to the existence of a  
 mutation in the peptidyl transferase. This cultivar also exhibited resistance  
 to the membrane-damaging properties of this toxin compared to the other  
 cultivar. This report summarizes the evidence for various kinds of '  
 \*\*\*trichothecene\*\*\* tolerance' mechanisms in fusarium head blight-resistant  
 wheat genotypes.

CONTROLLED TERM: Medical Descriptors  
 \*ribosome  
 wheat  
 cultivar  
 fusarium  
 protein synthesis inhibition  
 gene mutation  
 membrane damage  
 nonhuman

article

Drug Descriptors:

\*vomitoxin: TO, drug toxicity

phenylalanine

vegetable protein: EC, endogenous compound

peptidyltransferase: EC, endogenous compound

**trichothecene**

CAS REGISTRY NO.: (vomitoxin) 51481-10-8; (phenylalanine) 3617-44-5, 63-91-2;  
 (peptidyltransferase) 9059-29-4; (**trichothecene**)  
**51724-48-2**

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ACCESSION NUMBER: 95206038 EMBASE

DOCUMENT NUMBER: 1995206038

TITLE: Induction of cytokine mRNAs in mice after oral exposure to  
 the **trichothecene** vomitoxin (deoxynivalenol):  
 Relationship to toxin distribution and protein synthesis  
 inhibition.

AUTHOR: Azcona-Olivera J.I.; Ouyang Y.; Murtha J.; Chu F.S.; Pestka  
 J.J.

CORPORATE SOURCE: Dept. Food Science/Human Nutrition, Michigan State  
 University, East Lansing, MI 48824, United States

SOURCE: Toxicology and Applied Pharmacology, (1995) 133/1  
 (109-120).

ISSN: 0041-008X CODEN: TXAPA

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 026 Immunology, Serology and Transplantation  
 029 Clinical Biochemistry  
 052 Toxicology

LANGUAGE: English

SUMMARY LANGUAGE: English

## ABSTRACT:

The effects of oral exposure to 0, 5, and 25 mg/kg body wt vomitoxin (VT) on cytokine mRNA levels in spleen, Peyer's patches (PP), liver, kidney, and small intestine were evaluated in B6C3F1 mice at 2 and 4 hr postexposure using RT-PCR in conjunction with Southern hybridization analysis. The abundance of mRNAs for several cytokines was increased in VT-exposed mice with maximal effects occurring in the 25 mg/kg group at 2 hr. Specifically, IL-1 $\beta$  and IL-6 mRNA levels increased in spleen and PP following exposure to VT. TNF- $\alpha$  mRNA levels were markedly elevated in spleen and liver of VT-exposed mice. TGF- $\beta$  mRNA was increased in treatment kidneys and to a lesser extent in liver and small intestine. IFN- $\gamma$  mRNAs were elevated according to the rank order: spleen > PP > small intestine > liver > kidney, whereas IL-2 mRNAs were increased primarily in spleen and PP. VT had little effect on abundance of mRNAs for the TH2 cytokines, IL-4 and IL-5, or the housekeeping gene, hypoxanthine guanine ribosyl transferase. In order to relate cytokine mRNA abundance to toxin distribution, mice were administered 5 and 25 mg/kg VT body wt containing [3H]VT and tissue levels were monitored over time. Maximum VT molar equivalents for both doses were found at 30 min or 1 hr in all tissues with a rapid clearance following two-compartment kinetics over 24 hr. When effects of oral VT exposure on in vivo protein synthesis at 3 hr postexposure was measured using [14C]leucine uptake, it was found to be inhibited by  $\geq 20$  and  $\geq 50\%$  in tissues of mice receiving 5 and 25 mg/kg VT, respectively. While recovery was observed in tissues of the 5 mg/kg group at 6 hr, protein synthesis was still significantly inhibited ( $\geq 70\%$ ) at 9 hr for all tissues in the 25 mg/kg group. The results suggest that acute oral VT

exposure resulted in the transient elevation of mRNAs for proinflammatory and TH1 cytokines. These effects occurred immediately after peak VT accumulation and concurrently with marked in vivo protein synthesis inhibition.

CONTROLLED TERM: Medical Descriptors:  
\*protein synthesis inhibition  
\*toxicokinetics  
animal experiment  
animal model  
article  
controlled study  
kidney  
liver  
macrophage activation  
male  
mouse  
nonhuman  
small intestine  
spleen  
Drug Descriptors:  
\*cytokine: EC, endogenous compound  
\*trichothecene: TO, drug toxicity  
\*vomitoxin: TO, drug toxicity  
gamma interferon: EC, endogenous compound  
interleukin 1beta: EC, endogenous compound  
interleukin 4: EC, endogenous compound  
interleukin 5: EC, endogenous compound  
interleukin 6: EC, endogenous compound  
tumor necrosis factor alpha: EC, endogenous compound  
CAS REGISTRY NO.: (trichothecene) 51724-48-2; (vomitoxin)  
51481-10-8; (gamma interferon) 82115-62-6

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ACCESSION NUMBER: 93150395 EMBASE  
DOCUMENT NUMBER: 1993150395  
TITLE: Topical application of T-2  
toxin inhibits the contact hypersensitivity  
response in BALB/c mice.  
AUTHOR: Blaylock B.L.; Kouchi Y.; Comment C.E.; Pollock P.L.;  
Luster M.I.  
CORPORATE SOURCE: Environmental Immunology Section, NIEHS, P.O. Box  
12233, Research Triangle Park, NC 27709, United States  
SOURCE: Journal of Immunology, (1993) 150/11 (5135-5143).  
ISSN: 0022-1767 CODEN: JOIMA3  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ABSTRACT:

T-2 toxin, a trichothecene mycotoxin, has previously been shown to alter immune functions and promote skin tumors. We demonstrate that topically applied T-2 toxin reduces the ear swelling response to oxazolone challenge in BALB/c mice. For this reduction in ear swelling to occur, toxin application must be at, or within, 1 h after challenge. Dose-response studies showed a 44% reduction in ear swelling with 30 ng of T-2 toxin as compared

with a similar reduction with 300 ng of dexamethasone. **T-2**  
**\*\*\*toxin\*\*\*** did not affect Ag transport from the challenge site to the draining lymph nodes as measured by FITC transport. However, **T-2**  
**\*\*\*2\*\*\*** **toxin** significantly reduced both MHC class II (Ia) expression and Ag presentation at the same concentrations. Because **T-2**  
**\*\*\*2\*\*\*** **toxin**, a known protein synthesis inhibitor, was found to inhibit protein synthesis in epidermal cell cultures as measured by [3H]leucine incorporation, cycloheximide was also examined. Cycloheximide reduced both oxazolone-induced ear swelling and Ag presentation in a similar manner to **T-2**  
**\*\*\*T\*\*\*** - **2 toxin**. One mechanism of action for **T-2 toxin** in reducing the contact hypersensitivity response is via inhibition of protein synthesis and effective Ag presentation by epidermal Langerhans cells. This may involve alterations in Ia Ag expression, although a role for class II in the induction phase of the contact hypersensitivity response has not been established definitively.

CONTROLLED TERM: Medical Descriptors:  
 \*contact allergy  
 \*immune response  
 animal experiment  
 antigen expression  
 article  
 dose response  
 edema  
 immunomodulation  
 langerhans cell  
 male  
 mouse  
 nonhuman  
 priority journal  
**protein synthesis inhibition**  
 provocation test  
 Drug Descriptors:  
 \*t 2 toxin  
 cycloheximide  
 major histocompatibility antigen class 2: EC, endogenous compound  
 oxazolone  
 CAS REGISTRY NO.: (t 2 toxin) 21259-20-1;  
 (cycloheximide) 642-81-9, 66-81-9

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ACCESSION NUMBER: 93318701 EMBASE  
 DOCUMENT NUMBER: 1993318701  
 TITLE: Effect of emetine on **T-2 toxin**  
 -induced inhibition of protein synthesis in mammalian cells.  
 AUTHOR: Leatherman D.L.; Middlebrook J.L.  
 CORPORATE SOURCE: Toxinology Division, U.S. Army Medical Research Institute, Frederick, MD 21701-5011, United States  
 SOURCE: Journal of Pharmacology and Experimental Therapeutics, (1993) 266/2 (741-748).  
 ISSN: 0022-3565 CODEN: JPETAB  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 030 Pharmacology  
 037 Drug Literature Index

052 Toxicology

LANGUAGE: English

SUMMARY LANGUAGE: English

## ABSTRACT:

Chinese hamster ovary cells were used to examine the effect of emetine upon the toxicity of **T-2 toxin** and several related **\*\*\*trichothecene\*\*\*** inhibitors of polypeptide synthesis. Emetine inhibited protein synthesis and **T-2 toxin**- cell association in a concentration-dependent manner. The dose-response curves for these two effects were nearly identical. Over a narrow concentration range (0.3-3.0 µg/ml), emetine's inhibition of protein synthesis was partially reversible, whereas its inhibition of toxin-cell association was maintained for extended periods. This sustained inhibition of toxin-cell association, resulted in 'desensitized' cells with reduced sensitivity to the inhibitory effects of **\*\*\*T\*\*\* -2 toxin** on protein synthesis. Similar results were obtained when emetine-preincubated cells were challenged with diacetoxyscirpenol, verrucarol A and roridin A. In contrast, there were no measurable effects of emetine upon the response of the cells to the less potent **\*\*\*trichothecenes\*\*\***, deoxynivalenol, T-2 tetraol and verrucarol. In addition to emetine, several other inhibitors of polypeptide synthesis were examined for their effects on **T-2 toxin**-cell association and sensitivity to **T-2 toxin**. Of these, only cycloheximide inhibited toxin-cell association. Unlike emetine, sustained protection against the effects of **T-2 toxin** was not observed with cycloheximide.

## CONTROLLED TERM:

Medical Descriptors:

**\*protein synthesis inhibition**

animal cell

article

cho cell

controlled study

cytotoxicity

dose response

nonhuman

priority journal

protein synthesis

Drug Descriptors:

**\*emetine: CM, drug comparison****\*emetine: PD, pharmacology****\*t 2 toxin: TO, drug toxicity**

cycloheximide: CM, drug comparison

cycloheximide: PD, pharmacology

diacetoxyscirpenol: TO, drug toxicity

roridin a: TO, drug toxicity

verrucarol derivative: TO, drug toxicity

vomitoxin: TO, drug toxicity

## CAS REGISTRY NO.:

(emetine) 316-42-7, 483-18-1; (**t 2****toxin**) 21259-20-1; (cycloheximide) 642-81-9,

66-81-9; (diacetoxyscirpenol) 2270-40-8; (roridin a)

14729-29-4; (verrucarol a) 3148-09-2; (vomitoxin)

51481-10-8

## COMPANY NAME:

Sigma (United States)

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ACCESSION NUMBER: 92301828 EMBASE

DOCUMENT NUMBER: 1992301828  
TITLE: The toxicity of macrocyclic **trichothecenes**  
administered directly into the rat brain.  
AUTHOR: Bergmann F.; Yagen B.; Jarvis B.B.  
CORPORATE SOURCE: Department of Pharmacology, School of Pharmacy, Hebrew  
Univ.-Hadassah Medical School, Jerusalem 19010, Israel  
SOURCE: Toxicol, (1992) 30/10 (1291-1294).  
ISSN: 0041-0101 CODEN: TOXIA6  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 008 Neurology and Neurosurgery  
052 Toxicology  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ABSTRACT:

The tested macrocyclic **trichothecenes** are produced by Myrothecium fungi and by the plant Baccharis megapotamica. The toxicity of five macrocyclic **\*\*\*trichothecenes\*\*\*** has been measured by intracerebral and subcutaneous injection into rats. It is assumed that the toxic effects are based on inhibition of protein synthesis. Intoxication of rats by these compounds finds expression in slowly progressing respiratory depression and paralysis of skeletal muscles. The macrocyclics are derived from verrucarol, which lacks ring D and exhibits only low toxicity. The high toxicity of the macrocyclics, established by intracerebral and subcutaneous applications, may thus be attributed to the presence of the large ring D.

CONTROLLED TERM: Medical Descriptors:  
\*protein synthesis inhibition  
animal experiment  
article  
ld 50  
nonhuman  
paralysis  
rat  
respiration depression  
Drug Descriptors:  
\*trichothecene: TO, drug toxicity  
CAS REGISTRY NO.: (trichothecene) 51724-48-2

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